APRIL, 1950

The Review of Gastroenterology

OFFICIAL PUBLICATION

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

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VOLUME 17 NUMBER 4

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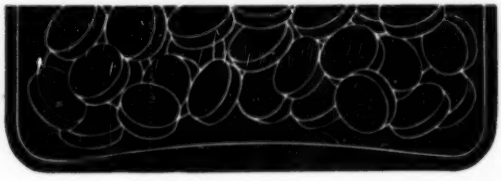

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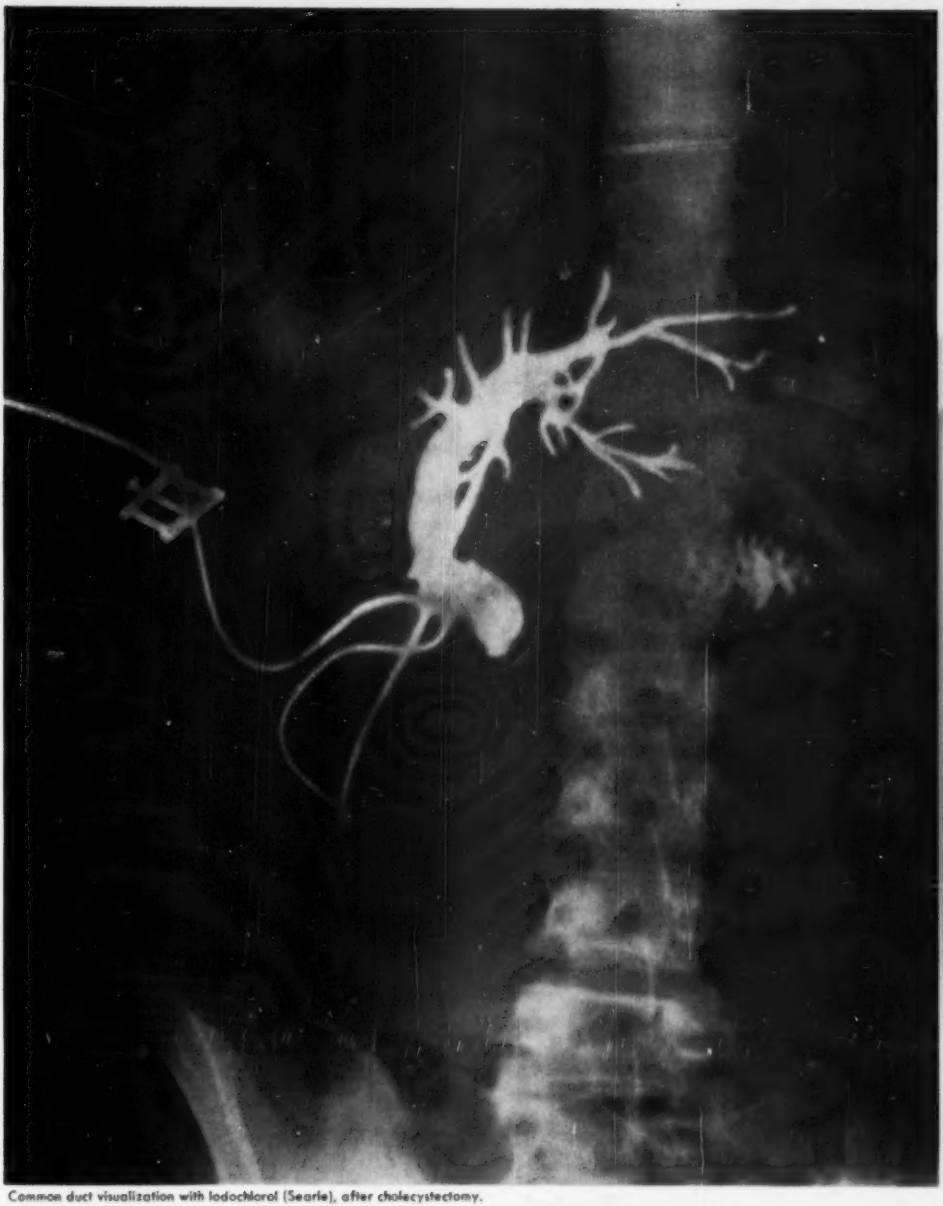

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(INCORPORATING THE AMERICAN JOURNAL OF GASTROENTEROLOGY)

The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

VOLUME 17 APRIL, 1950 NUMBER 4

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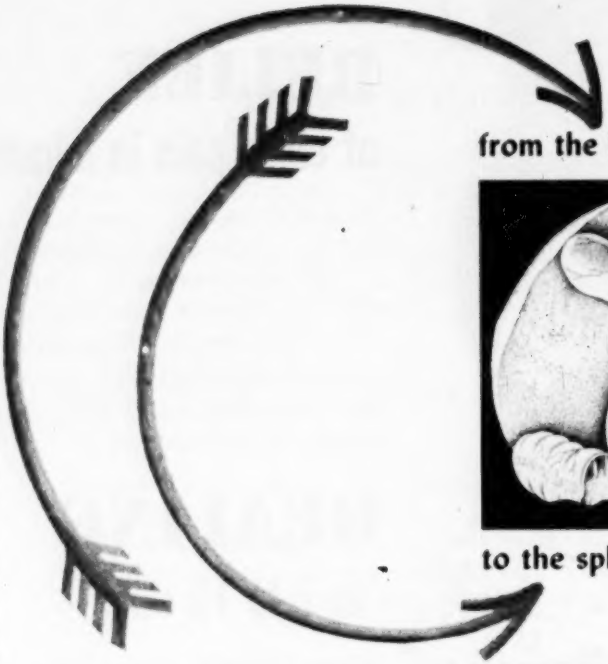

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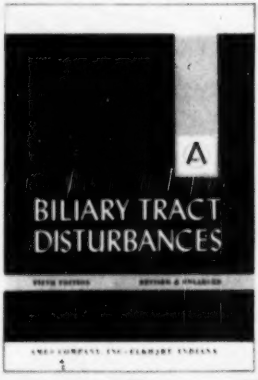

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BEZOAR: REPORT OF THREE CASES*

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Human bezoars are relatively rare and interesting medical findings. The term "bezoar" can be loosely defined as a concretion of various character in the stomach or intestines of humans and other animals. During Antiquity, through the Middle Ages, and up to the 18th century, the bezoar was considered to have remarkable protective and curative powers and as such played an important role in medical practice. Bezoar stones from goats' stomachs were used as a remedy by the Hindus as far back as the 12th Century B.C. During the Middle Ages the bezoar was looked upon with reverence and awe; the concretion was often encased in precious metal caskets and carefully handed down to succeeding generations. As would be expected the supposedly protective and remedial powers of the bezoar were used against many types of malady. It was considered an excellent remedy for snake poisoning, dysentery, leprosy, dizziness, blindness, sexual impotence, and a host of others. As a consequence of the high value of a good bezoar, imitations and counterfeits soon appeared on the market and various trials were devised to distinguish the genuine article from the fraudulent—e.g.—

(1) Pierce the stone with a red hot needle. If it is genuine there will be no smoke. (2) Administer poison to an animal or man, and give powder made from the stone as a remedy. If the individual survives, the stone is genuine. (3) Triturate the stone with saliva or with water. If it is genuine it will discolor a cloth.

Much of the material in the preceding introduction can be found in the excellent article by Matas[1] in Transactions of the Southern Surgical and Gynecological Association in 1914. For a more detailed and complete account of the historical background of bezoars, the reader is referred to this article.

The bezoar presents a relatively uncommon surgical problem. In 1914 Matas was able to collect 73 authenticated cases in which the presence of a bezoar was confirmed at autopsy or at operation. In an exhaustive search of the world's literature up to 1938, Ochsner and DeBakey[2] were able to collect a total of 303 cases to which they added eight of their own, making a grand total of 311 cases.

*From the Gastric Service, Memorial Hospital, New York, N. Y.

Bezoars occurring in humans can usually be classified in one of the same following groups:

(1) *Trichobezoar*—The bezoar is composed almost entirely of ingested human hair.

(2) *Phytobezoar*—The bezoar is composed largely of vegetable matter. For practical purposes this group can be subdivided into:

(a) bezoars composed of persimmons. Ochsner and DeBakey suggest the term "diospyrobezoar" for these.

(b) bezoars composed of other vegetable matter. This includes bezoars composed of celery, pumpkin, heather twigs and roots, grape stems, prunes, raisins, etc.

(3) *Concretions*—These are unusual types of bezoars and occur chiefly in people who ingest furniture polish for its alcoholic content. The polish consists of an alcoholic solution of shellac and the addition of water to this causes a viscous precipitate to form.

Of the 311 cases collected from the world's literature up to 1938 by Ochsner and DeBakey, the incidence of the various types was as follows:

Trichobezoars—		172
Phytobezoars—		126
(a) diospyrobezoars—	92	
(b) other phytobezoars—	34	
Concretions—		13

Age and sex differences are strikingly apparent in the two large group of bezoars. Trichobezoars occur approximately 10 times more frequently in females. The highest incidence of trichobezoar is found in the 10-19 year age group. Slightly more than 33 per cent of all cases are found in this group. Phytobezoars, on the other hand, are more frequent in males in the ratio of 3/1. The peak incidence for phytobezoar is in the 5th decade. Slightly more than 25 per cent of cases occur in this group.

Etiology

Trichobezoars:—A discussion of the etiology of trichobezoars seems to center on two points. First, the reason for trichophagia and, secondly, why, after ingestion of hair, does the hair tend to accumulate in the stomach. As far as the first point is concerned Matas suggests that the far greater incidence in the female sex might be due to the prevailing custom of girls wearing their hair long with consequent easy accessibility in an individual with an inclination to chew her hair. The prevailing opinion at present is that trichophagia is a manifestation of some underlying personality disturbance. As such it might be placed in the same classification as thumb-sucking or nail-biting. The initial problem of trichophagia seems then to be a psychiatric one. The habit may be one of long standing and there are cases on record where trichophagia occurred over a period of 22 years.

The second point—why the ingested hair remains in the stomach—is still an enigma. One can conceive of a small number of hairs becoming stuck in a folded over portion of gastric mucosa and not being passed through the pylorus. No satis-

factory explanation has been given as to the stomach's inability, through peristalsis, to advance the small hair ball through the pylorus. On occasion the hair balls, while still small, pass through the pylorus. Watt and Harner[3] have reported 3 cases of acute intestinal obstruction from bezoars, but the fact remains that the great majority remain in the stomach.

Phytobezoars:—About 75 per cent of phytobezoars are properly diospyrobezoars or persimmon bezoars. These bezoars have a distinct geographical distribution and are confined largely to the southern part of the United States and Japan where persimmon trees are abundant. As with trichobezoars there have

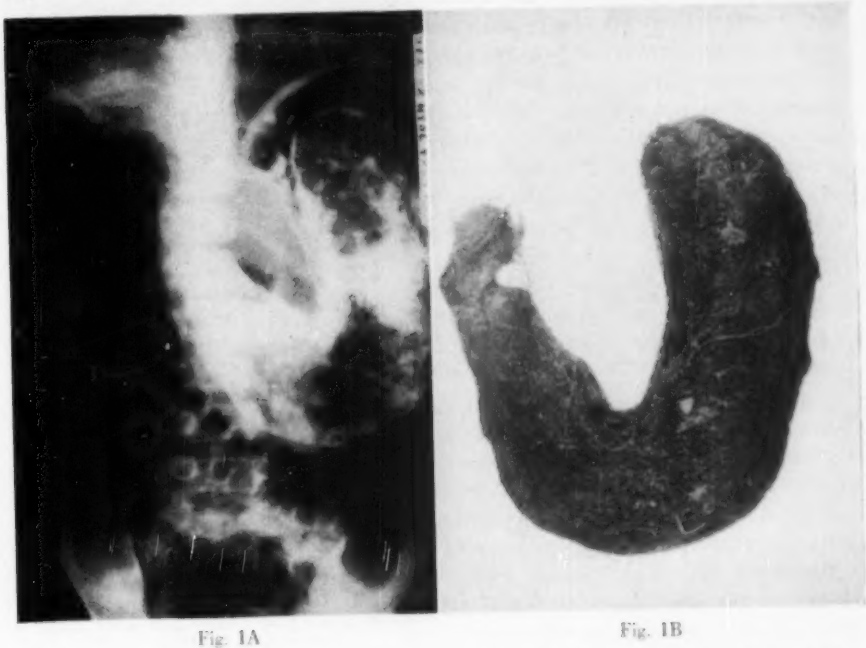

Fig. 1A Fig. 1B

Fig. 1—Case 1. Trichobezoar. A. Roentgenogram of stomach. B. Photograph of gross specimen.

been numerous speculations as to the etiology of phytobezoars. However, with regard to the latter, there is a fairly plausible chemical explanation which sheds some light on their formation. The most interesting and the best explanation to date comes from the work of Izumi[4] et al in Japan. Persimmons contain soluble shibuol which is a phlobatannin composed of phloraglucin and gallic acid. Soluble shibuol is precipitated by dilute mineral acids such as HCl. With this fact in mind Izumi incubated small pieces of persimmon fruit with the various digestive juices and found that only with gastric juice could they produce rather typical persimmon bezoars. They conclude that the sticky precipitate of shibuol serves as a glue which binds the pieces of fruit, skin, and seeds together.

Symptomatology:—The symptoms induced by bezoars do not fall into a nice pattern. What symptoms do exist are often vague and misleading and are easily mistaken for many other intraabdominal conditions. One of the outstanding features seems to be the frequency with which an individual harboring a huge bezoar over a period of years may suffer only from vague dyspepsia and remain in a fairly good nutritional state. In the cases collected by Ochsner and DeBakey epigastric pain was the most frequent symptom and occurred in 70.2 per cent of cases. There is absolutely nothing characteristic about this pain. It runs the gamut from a vague, dull, aching sensation to a sharp, burning pain. There is no constant relation to meals. Nausea and vomiting (64.4 per cent), weakness and loss of weight (38.1 per cent); and constipation alternating with diarrhea (32 per cent) were the next most frequent symptoms (Ochsner and DeBakey).

Diagnosis:—The possibility of trichobezoar should be entertained in the presence of an upper abdominal mass in an adolescent girl who does not appear particularly ill. Both patient and family should be closely questioned as to any evidence or observation of trichophagia in the past. A dietary history of persimmon ingestion in a middle-aged male might arouse a suspicion of diospyrobezoar, but in this age group the diagnostician is more concerned about the possibility of ulcer or gastric cancer.

Physical examination reveals the presence of an abdominal mass in the majority of cases. The abdominal tumor frequently has the shape of the stomach. A few other helpful distinguishing features are the wide range of mobility of the tumor, the uniform firm consistency, and the smooth surface.

Laboratory studies are in no way diagnostic. Occasionally a clue is furnished by the regurgitation of bits of hair; gastric washings may bring up bits of hair. By far the greatest single aid in the diagnosis of bezoar is x-ray study of the stomach. Matas stated that in 1911 prior to the use of systematic x-ray study in suspected cases, the correct preoperative diagnosis was made in only 10 out of 44 cases. In the remainder exploratory laparotomy was performed for admittedly undiagnosed abdominal tumors. Following the introduction of barium meals in suspected bezoars the percentage of cofrect preoperative diagnoses increased to about 70 per cent. More recently gastroscopy[5, 6, 7] has begun to play an important role in the diagnosis.

Treatment:—The only effective treatment is surgical, i.e., gastrotomy with removal of the bezoar. Even this procedure may not always deter an individual who is bent on eating hair; in a report by Harris[8], a patient submitted to 5 gastrotomies for recurrent hair-ball.

In spite of the seemingly innocuous clinical course in these patients, there is a considerable mortality in those not subjected to operation. As Matas puts it—"Alternating attacks of constipation and diarrhea are the usual rule. Eventually the breath becomes exceedingly foul and offensive; anemia grows more pronounced; ingestion of food more difficult; emaciation and exhaustion more noticeable and, unless surgical measures are instituted, with rare exception death occurs from inanition or perforation."

Ochsner and DeBakey report the following mortality figures from collected cases:

	Trichobezoar	Diospyrobezoar	Other Phytobezoars
Unoperated	72.7 per cent	50.0 per cent	66.6 per cent
Operated	4.8 per cent	7.4 per cent	4.7 per cent

Report of Three Cases

There have been three cases of bezoar seen and operated upon at Memorial Hospital. There were two cases of trichobezoar and one case of phytobezoar. As one would expect in view of the foregoing discussion, the trichobezoars occurred

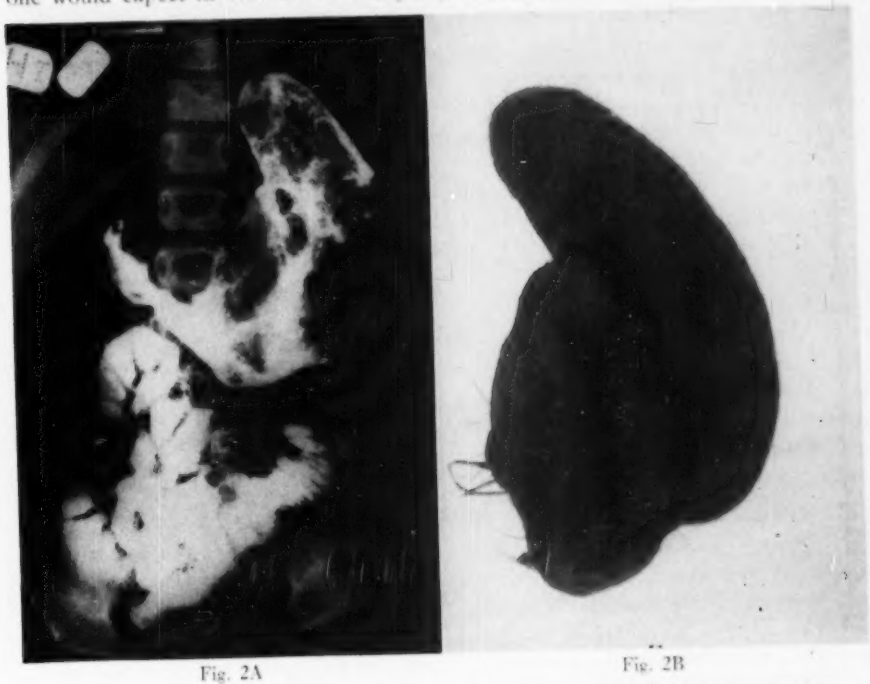

Fig. 2A Fig. 2B

Fig. 2—Case 2. Trichobezoar. A. Roentgenogram of stomach. B. Photograph of gross specimen.

in young girls. The phytobezoar occurred in a 50-year-old man who gave a long history of persimmon ingestion.

In each case gastrointestinal symptoms were of a mild, indefinite nature. In two of the cases there was a palpable, freely movable, upper abdominal mass. The preoperative diagnosis of bezoar was made in each case by the radiologist following gastrointestinal x-ray study. Confirmation of the radiographic diagnosis of bezoar was made in the third case by means of gastroscopy which revealed the presence of a dark green movable ball in the stomach.

Case 1:—M. B., 91664, Memorial Hospital, admitted Aug. 8, 1948, discharged Aug. 24, 1948.

Chief Complaint:—Mass in left upper abdomen of three weeks duration.

The patient is a three-year-old girl. The child was a full-term baby. Early growth and development were apparently normal. Three weeks before admission to the hospital the child developed puffy red eyes, red throat and fever of 103° F. Urinalysis and blood counts were reported as normal. No specific treatment was given and the child recovered completely. During this illness the examining physician detected a mass in the left upper quadrant of the abdomen. For a week prior to hospital admission the patient complained of inconstant upper abdominal pain on several occasions, but was otherwise asymptomatic. Appetite was good and there was no weight loss. No nausea or vomiting. No change in bowel habits. No diarrhea or melena. No urinary frequency, dysuria, pyuria, hematuria.

Physical Examination:—The patient was an alert, friendly three-year-old child who did not appear ill. In the left upper quadrant and extending downward and medially there was a firm non-tender mass the contour of which appeared to conform to that of the stomach. The tumor was movable on palpation and descended with inspiration. The inferior border of the mass was smooth. The superior limits of the tumor could not be outlined, because of the overlying costal margin. The liver was not palpable and no other abdominal masses of tenderness were found.

Laboratory Data:—Temperature 99; Pulse 90; Respiration 20; Blood pressure 90/65; Hemoglobin 13.7 gm.; WBC 7.2 with normal differential count. Urinalysis: Within normal limits. No significant findings.

Radiographic Examinations:—*I. V. Pyelograms*:—Following diodrast injection the renal pelves, calyces and ureters on both sides were clearly outlined and presented a normal appearance.

Chest Plate:—Normal cardiac shadow and clear lung fields.

Gastrointestinal and Colon Studies:—Air studies of the colon showed the latter to be situated below the mass and entirely independent. Following oral ingestion of barium a definite defect was observed in the stomach. On fluoroscopy the radiologist was not certain whether this defect was due to extrinsic pressure or to an intrinsic mass largely filling the lumen of the stomach. Following study of the films it was felt that the mass was intrinsic and a diagnosis of bezoar was made.

Operation:—On 8/16/48 a gastrotomy was done under ether anesthesia and a large trichobezoar was removed. The bezoar resembled closely a cast of the stomach.

Comment:—Questioning of the child's mother and grandparents brought to light some pertinent information: At the age of 10 months the child had a severe alopecia which was attributed to a vitamin deficiency. However, the amount of hair recovered was never sufficient to account for the amount lost. The mother also stated that "she ate the fuzz off woolen blankets and also chewed on furry objects". During the postoperative period the child was observed closely by the nurses for evidence of trichophagia, but none was detected. One morning, however, chewed and matted balls of string were found in the child's bed. The postoperative course was uneventful. On discharge the child was placed in the care of a psychiatrist.

Case 2:—P. P., 77921, Memorial Hospital, admitted June 14, 1945, discharged July 8, 1945.

Chief Complaint:—Abdominal pain.

Unfortunately the parents of this child were not available to give a complete history and the child's only complaint was abdominal pain. No weight loss, vomiting, diarrhea, bloody or tarry stools. The child admitted that she liked to chew on her hair and fingernails.

Physical Examination:—The patient was an eleven-year-old white female who appeared chronically ill. Skin and mucous membranes were pale. Essential physical findings were limited to the abdomen. In the left upper quadrant there

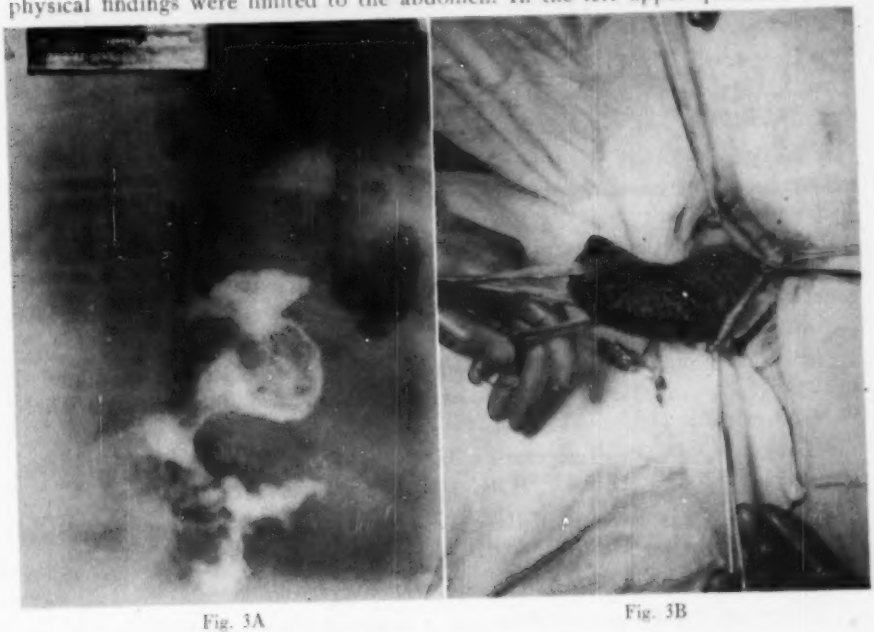

Fig. 3A Fig. 3B

Fig. 3—Case 3. A. Roentgenogram of stomach. B. Extraction of bezoar through gastrotomy.

was a firm, freely movable tumor. The superior margin could not be felt because of the costal margin. Inferiorly and medially the mass extended a short distance across the midline just above the umbilicus.

Laboratory Data:—Temperature 98.8; Pulse 100; Blood Pressure 120/80; Hemoglobin 11.6 gm.; RBC 3.9; WBC 6.3 with normal differential. Urine examination was normal.

Radiographic Examinations:—Gastrointestinal series revealed a large polypoid mass extending into the fundus of the stomach. Normal mucosal pattern was seen only in the extreme upper portion of the fundus. The mass was large and there appeared to be a fairly wide attachment to the midportion of the lesser

curvature. The prepyloric region and the duodenum, appeared normal. There was no delay in emptying time. The radiologist's impression was that the mass was suggestive of a bezoar, but that a benign tumor of the stomach such as leiomyoma should be considered.

Chest plate and Intravenous Pyelograms were normal.

Clinical Course:—On 6/25/45 a gastrotomy was performed under GOE anesthesia. A large black, hairy tumor measuring 15 x 9 x 5 cm. was removed. There was considerable superficial ulceration of the mucosa of the lesser curvature. The postoperative course was normal and the child was discharged on the 13th postoperative day. Unfortunately the child has been lost to follow-up observation and her subsequent course is not known to us.

Case 3:—J. R., 52372, Memorial Hospital, admitted May 21, 1944, discharged June 5, 1944.

Chief Complaint:—Loss of weight and constipation.

Six months before the first clinic visit, this patient developed anorexia and constipation. There was no vomiting, bloody or tarry stools. On rare occasions he had slight epigastric pain, but this was never incapacitating. He lost 15 pounds during the six months period prior to the clinic visit. The patient had been treated (on the outside) by two physicians who prescribed patent medicines with no relief of symptoms. A history of persimmon ingestion was obtained from the patient.

Physical Examination:—The patient was a fifty-year-old male who appeared in fairly good health. General physical examination revealed nothing of note. There were no palpable abdominal masses.

Laboratory Data:—Temperature 37 C.; Pulse 80; Blood Pressure 130/90; Hemoglobin 12 gm.; RBC 4.0; WBC 11.4 with normal differential count.

Urinalysis was normal. Blood Chemical Analyses—Proteins 6.8; Chlorides 101; BUN 10.5. Gastric Analysis—93 units of free acid (maximum).

Radiographic Studies:—*Barium Enema*:—Negative.

Gastrointestinal series:—There was a rounded mass apparently free in the gastric lumen and which could be readily moved around. There was also constant narrowing of the antral end of the stomach, but no ulcer crater was demonstrated. A radiographic diagnosis of gastric bezoar and chronic duodenal ulcer was made.

Gastroscopy:—There was a spherical dark green foreign body seen in the stomach.

Course:—The patient was advised to enter the hospital, but he refused and accordingly he was treated in the clinic as an outpatient for five months. During this period his symptoms remained relatively unchanged. In May of 1944 he suddenly decided that he wished the operation. He was admitted to the hospital and on 5/23/44, a gastrotomy was performed under spinal anesthesia and a greenish-black phytobezoar measuring about 4 x 3 x 3 cm. was removed. Inspection of the gastric mucosa at operation revealed multiple superficial gastric ulcers

presumably resulting from irritation. Section of the bezoar revealed spongy, necrotic, friable material with a sickening sweet odor.

The postoperative course was uneventful. On discharge he was cautioned about eating persimmons. He has been followed closely with repeated G.I. Series and when last seen in January, 1948, he was asymptomatic.

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TRANSPLEURAL BILATERAL VAGOTOMY WITH RESECTION OF THE TENTH NERVES*

WILLIAM REID MORRISON, M.D.†
and
STANLEY MIKAL, M.D.**
Boston, Mass.

Bilateral vagotomy, with or without resection of the tenth cranial nerves, is a comparatively new operation for peptic ulcers and may be performed either through the abdomen or left chest. It is particularly used in selected cases of duodenal or jejunal ulcers. Over a thousand vagotomies have been reported in the literature.

The majority of surgeons and medical men agree that the operation has been most successfully used in cases of stomal or jejunal ulcers which followed partial gastrectomy or gastroenterostomy.

Nonobstructing intractable duodenal ulcers, gastric ulcers high on the lesser curvature of the stomach, cardioesophageal ulcers and ulcers of the lower third of the esophagus are also considered by some surgeons as indications for this operation.

Subtotal gastrectomy, with or without vagotomy, should be performed for recurrent or intractable gastric ulcers because of the high incidence of malignancy in these cases.

Bleeding duodenal ulcers, preferably in the interval between hemorrhages, persistent postoperative abdominal pain following gallbladder or pancreatic disease, and intractable pain of intraabdominal carcinomatoses, have also been treated successfully in many instances by vagotomy. Even the elimination of abdominal pain following alcoholic sprees has been reported by some authors after vagotomy.

Patients who require surgical treatment of their peptic ulcer and who refuse partial or complete gastrectomy, often permit vagotomy because it is a less formidable procedure.

Contraindications for vagotomy are: obstruction from activity and scarring of an ulcer at or near the pylorus, and any question of malignancy of the stomach or duodenum. It is also contraindicated in patients with hypertension and those who have undergone thoracolumbar sympathectomy for hypertension, because of the danger of further elevating the blood pressure.

Peptic ulcers about to perforate or bleed are not affected by vagotomy. A patient may perforate or bleed before, during or after vagotomy.

Several reports of "painless" or "silent" perforations of peptic ulcers after vagotomy have appeared in the literature. It should be remembered, that the vagus nerve does not carry pain fibres and therefore, its section cannot abolish

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pain. Vagotomy simply relieves ulcer pain indirectly by decreasing gastric acidity and gastroduodenal spasm.

Some fifteen years ago, I was the first surgeon at the Boston City Hospital to remove the whole stomach successfully for carcinoma involving both cardiac and pyloric regions of the stomach. An end-to-side anastomosis was performed between the esophagus and jejunum through the abdomen. Secondarily, both tenth nerves were sectioned in doing this complete gastrectomy.

In performing transpleural vagotomy, a segment of both tenth nerves is resected for pathological indentification, and to prevent reunion of the nerve trunks. The transpleural approach gives better exposure of the esophagus and the tenth nerves, thereby making section of both nerves and their plexuses more certain and complete. Marked differences in the size, shape, and position of these tenth nerves, as well as their connecting branches on and near the esophagus have been noted.

The most acceptable indication for transthoracic vagotomy is extensive intra-abdominal adhesions and jejunal ulcer which may result from subtotal gastrectomy or gastroenterostomy.

The main disadvantage of the transthoracic approach is the inability to inspect and palpate intraabdominal organs, but this may be obviated by opening the diaphragm. If adhesions bind the lung to the diaphragm or parietal pleura, they are severed so that the lung may be retracted to expose the esophagus. If dense, firm and extensive adhesions are present between the lung and diaphragm, an incision is made into the peritoneal cavity through the chest and a transabdominal vagotomy performed. If dextrocardia is present, the right chest should be opened. During the routine examination of sixty thousand chest x-rays in the U. S. Navy, Mikal found dextrocardia present in two-tenths per cent of the cases.

Perforation of the esophagus has been reported in the course of dissecting the tenth nerve trunks. Complications of chest surgery which may follow transthoracic vagotomy, namely, hydrothorax, pneumonitis, atalectasis, hemothorax and pneumothorax, are usually transient.

The favorable results of vagotomy are: lessened gastric peristalsis, marked decrease in gastric acidity and secretion, relief of epigastric pain, and a sense of well being. An improved appetite is noted by the patient. The patient gains weight, returns to work, sleeps well, and is surprised that formerly forbidden fruits, tomatoes, etc., may be eaten without unfavorable symptoms.

In many cases, atony and sluggish peristalsis of the stomach occurs. Atony of the stomach with distention to twice normal size has been noted. The use of a gastric tube relieves this distention. Nature eventually accommodates itself to the lessened peristalsis, and there is no need of a supplementary gastroenterostomy when a patent pylorus is present, for within six to twelve months, the stomach assumes its normal size, shape and tone, and resumes active peristalsis.

Other complications of vagotomy have been occasional diarrhea for a period of weeks or months, and reports of difficulty in swallowing have appeared in the

literature. If digital manipulation of the esophagus is performed, and no instrument or rubber tubing is used to retract the esophagus into the left chest, this difficulty in swallowing is obviated.

Postoperative intercostal neuralgia is usually controlled by injection of nupercain in oil into the intercostal nerves either at the time of operation or subsequently. Patients are usually up and about the day after operation, and liquids and soft solids are given the next few days, followed by a house diet. Penicillin is given in amounts up to 100,000 units or more every three to six hours.

About half of our cases were placed on Wangensteen suction for one to five days after vagotomy. Of twenty-three patients not on suction, six developed gastric dilatation or other gastrointestinal symptoms. Of those on suction, ten subsequently developed belching, nausea, vomiting, diarrhea or distention. Hence, postoperative suction did not appear to prevent the aforementioned symptoms.

The insulin test was found to be reliable in testing the completeness of vagus section, but was unreliable in predicting the end results of the operation.

Forty-seven vagotomies have been performed at the Boston City Hospital by various surgeons during the last four years. I operated on a majority of these cases and had no mortality. However, two patients have died in this hospital series: one with a coronary occlusion and myocardial infarction at thirty-eight years of age, and the other of extensive carcinomatosis. Both of these diagnoses were verified by autopsy. Another transpleural vagotomy which I performed elsewhere, developed partial collapse of the lung and later died after undergoing an abdominal jejunostomy by an out-of-town surgeon.

In this series of cases there were twenty-four nonobstructing benign ulcers of the duodenum, two obstructing ulcers of the duodenum, eleven stomal ulcers, and three gastric ulcers. Seven patients had both benign duodenal and gastric ulcers.

Most of the patients with benign nonobstructing duodenal ulcers had their ulcer symptoms for ten to twenty years.

Of the forty-seven patients, thirteen had a previous history of one or more perforations, while twenty-seven had one or more episodes of bleeding. Perforation occurred in six duodenal ulcers, five gastric ulcers, and one stomal ulcer. Simple closure of the perforation was performed in each case. Of the bleeding ulcers, ten were duodenal, six stomal, and two associated gastroduodenal ulcers. In the latter, it was not known whether the gastric or duodenal ulcer bled.

Twenty-two patients had a total of twenty-seven previous gastrointestinal operations. Twelve had closure of perforated ulcers, ten had subtotal gastrectomy and five had gastroenterostomy.

Transthoracic vagotomy was performed in thirty-eight cases and transabdominal vagotomy in eight cases. In one case an abdominothoracic approach was used. Whenever a segment of rib is removed in performing transthoracic vagotomy, it is cut into several pieces and placed in a sterile jar in the deep freeze of the bone bank for future bone grafting on the Bone and Joint Service of the hospital.

Complementary subtotal gastrectomy was performed in three cases and gastroenterostomy in three cases of the eight cases treated by transabdominal vagotomy.

Of thirty-eight patients having the transthoracic operation, twenty-eight developed chest complications mostly to a mild degree.

Unfavorable results which followed transpleural vagotomy with resection of both nerves were: 1) duodenal obstruction in two patients, one of whom was treated by gastric resection, and the other by posterior gastroenterostomy and 2) stomal ulcers after vagotomy in two patients, one of whom had a subsequent resection. One patient had recurrent episodes of bleeding after vagotomy and was subjected to subtotal gastrectomy. These failures occurred for the most part in chronic alcoholics with poor dietary habits which could account for bleeding and recurrence of an ulcer or the development of a new ulcer.

Patients who develop a jejunal ulcer after partial gastrectomy, may be treated by a higher gastric resection. Despite this second gastrectomy, cases have been reported where a jejunal ulcer or another gastric ulcer has developed necessitating, possibly, a complete gastrectomy. Vagotomy with resection of both nerves might well be performed in patients with such an ulcer diathesis to attempt to avoid multiple gastrectomies and total gastrectomy with their consequent higher morbidity and mortality rates.

PRESENT STATUS OF FLEXIBLE TUBE ESOPHAGOSCOPY*

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In June 1947, at the annual meeting of the American Medical Association, a flexible esophagoscope was presented by the author, which, in his judgment, would revolutionize the accustomed instrumental approach in the diagnosis and treatment of disorders of the esophagus. The need for such an accomplishment is apparent, for prior to this time, the accessibility of this organ to diagnostic measures or therapeutic manipulation was as limited as it was confined by the two practical methods in common use—the roentgen ray and the rigid esophagoscope.

When Kussmaul[1] contributed his epoch making observations in 1868, an avenue of investigation was opened which gave promise of unbounded opportunities for research and the expansion of knowledge of this organ. Soon, other workers were drawn into the field. Among these notables were Mikulicz[2], a surgeon, and Killian[3], a laryngologist. The latter's energies brought about a close relationship of his specialty to endoscopy which has been maintained up to the present time. It is not unnatural therefore that esophagoscopy came to be regarded as a surgical procedure.

To be sure, the introduction of an esophagoscope has always been viewed as a serious undertaking, one not without its many dangers and frequent catastrophes. Its passage in the past has been limited to those who, as a result of intensive training and unusual skill, were able to carry out this difficult procedure. It is obvious, therefore and not at all surprising, that neither patient nor clinician would be overly enthusiastic in being the subject on the one hand or the motivator on the other, save for those extreme situations where there could be no alternative. An emergency such as a foreign body or need for biopsy has been the main field for esophagoscopic usefulness. The picture that lies before us with the use of the rigid tube was therefore one of fear and reservation. The performance itself was in every sense an operation, conducted in a surgical atmosphere with all its embellishments. Infrequency of instrumentation paralleled restraint. One is reminded of the few cases which internes actually witness during their hospital tenure, and then too they may have to go over to the Nose and Throat Department to observe them. Not that there is anything wrong in that, other than the feeling one may get, that the esophagus is so far removed when in reality it is so near. And this proximity has been maintained by the labors of Paulson and Benedict, amongst other gastroenterologists. Their expanded clinical horizons incorporated this instrumental phase within the framework of their gastroenterologic concepts and practice.

It is well to acknowledge that the profession's avoidance of esophagoscopic instrumentation has been more or less a universal practice. Even the most extra-

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ordinary technician could not dispel this resistance and attract to himself, if not to his coworkers as well, a cooperative interest in the more general application of this form of manipulation.

The perfection of x-ray diagnosis in the early part of the century has been a milestone in the acquisition of knowledge of the gullet. It wasn't long before both surgeon and clinician soon shared the confidence of the roentgenologist in a concerted reliance on this form of examination for both diagnostic and therapeutic purposes. The value of an esophagram is directly related to one's success in interpreting its silhouette or alteration of shadow. Unfortunately, because of anatomic reasons, the latter is dependent upon some form of obstruction or sacculation for its worth. Attempts[4] at thinning of the shadow producing contrast mixture has been resorted to. The x-ray serves well in the detection of anomalies, spasm, stenosis, neoplasm and in the recognition of peptic ulcer and varices. The importance of the roentgenologist's aid cannot be underestimated. Positive information is invaluable when obtainable. As in gastroscopy, the collaboration of the x-ray diagnostician with the endoscopist brings about that cooperation which only good teamwork can offer. Every endoscopy should be preceded by a careful roentgen survey. The latter cannot establish the existence of inflammation, mucosal ulceration, local points of bleeding, angioneurotic edema, scleroderma, tuberculosis, lues, nor differentiate with certainty between benign and malignant neoplasm. Therein lies the need for direct instrumental inspection of the esophageal lumen itself.

Anyone with a little training can introduce a flexible esophagoscope. The procedure is simple, safe and easy. The patient is not subjected to any ordeal. The intense surgical preparation, so indispensable in the use of the rigid tube has not been found necessary. No mental hazard besets the operator. There supervenes a feeling of confidence and accomplishment. These conclusions are the result of our experience in performing flexible esophagoscopy in over 400 patients. These included diagnostic surveys, removal of foreign bodies, dilatations for stricture, injection of varicosities, in addition to the performance of a few gastric biopsies upon deeper penetration of the instrument.

The preliminary preparation and technic has been amply described in previous publications[5, 6].

The safety factor resides in the soft spiral tip of the author's instrument. It is important to point out, that flexible tube esophagoscopy does not imply blind introduction. As soon as the pharyngeal barrier is transversed, visual guidance is immediately resorted to with simultaneous insertion of the scope into the deeper recesses. As withdrawal of the mechanism is attempted, inspection is similarly continued to insure a thorough and detailed survey.

It would be grievous if the impression were obtained that force or the disregard for asepsis would not give rise to trouble. Under no circumstances is rough handling to be countenanced. The anatomy and physiology of this organ must be respected. The wall of the esophagus is thin. Reckless attempts at the use of biopsy forceps, for example, may well cause a perforation of the viscus. A perfectly

simple and safe procedure could thus be transformed into a disastrous one. Specific contraindications to instrumentation must likewise be observed. Patients with fever, extreme debility, aneurysm, cardiac disorders, dyspnea would not be considered proper subjects. A high lying lesion is a contraindication to the use of the flexible esophagoscope. Such cases require direct visual guidance at the outset. These are, however, in the minority.

With the institution of this new form of esophageal technic, a method has been established which has enabled, in actual experience, a safety and simplicity of exploration quite unlike that which has hitherto been possible. The manifold disorders of this vital organ with its array of surrounding structure is brought within easy reach of the clinician and surgeon. No longer is there justification for avoiding this type of instrumentation. Inspection of the esophageal lumen can be carried out routinely and repeatedly, tissues may be removed for microscopic study, and treatment carried out if required. A once formidable procedure shrinks in its reality and can no longer be regarded as a deterrent to investigation and progress.

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INHIBITION OF THE ACTIVITY OF TRYPSIN BY ADSORPTIVE AGENTS

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Adsorptive agents have, in the course of years, found a real and permanent place in the practice of medicine. Charcoal, kaolin, aluminum hydroxide, magnesium trisilicate and, recently, resins form an essential part of the therapeutic armamentarium of the physician. Despite this wide usage of these agents, relatively little work has been done in the study of their broad activity in the gastrointestinal tract.

TABLE I

Adsorbent or Inhibitor	Results Obtained	Reference
Halides of Li, Na, K, and NH_4 in 0.5 M concentrations.	Depressed rate of tryptic digestion.	8
$CaCl_2$ and $MgCl_2$ in 0.0083 M concentration.	Inhibited the digestion of gelatin by trypsin. $CaCl_2$ more effective.	9
Zn, Hg, and Mn.	Inhibited tryptic activity.	10
Detergents, triacetin	Depress tyrosine production by trypsin from hemoglobin.	11
Anacardic acid in conc. 1:1000 to 1:100,000	Inhibited the digestion of casein by trypsin in vitro.	12
Ultraviolet light	Trypsin solutions lose activity.	13
Soaps (potassium)	Inhibited proteolytic action.	14
Magnesium citrate	Strongly inhibits pancreatic trypsin.	15
Bauxite, carborundum, and magnesium silicate.	Adsorb trypsin	16
Alcohol	Destroys tryptic activity in vitro and in vivo.	17

In an effort to extend knowledge in this field, work has been reported on the capacity of adsorptive agents to function in the following systems:

1. Inhibition of pepsin[1].
2. Inhibition of lysozyme[2].
3. Adsorption of putrefactive chemicals[3].
4. Adsorption of paralytic shellfish poison[4].
5. Adsorption of bacteria and bacterial toxins[5].

For a further step in the understanding of the action of adsorptive agents, it was deemed advisable to study the effects of these materials on the activity of

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TABLE II

Adsorbent	% adsorbed using 0.1 gm. adsorbent per 100 cc. Trypsin sol. (8 mg./100 cc.)	% adsorbed using 0.4 gm. adsorbent per 100 cc. of same trypsin solution.
1. Insoluble polyamine anion exchange resin A, commercial sample, 200 mesh.	none	none
2. Insoluble polyamine anion exchange resin B, commercial sample, 200 mesh chloride salt.	45	73.0
3. Insoluble polyamine anion exchange resin C, commercial sample, 200 mesh.	none	none
4. Insoluble polyamine anion exchange resin D, commercial sample, 200 mesh.	31.0	39.0
5. Insoluble polyamine anion exchange resin E, commercial sample, 200 mesh.	31.0	39.0
6. Insoluble polyamine anion exchange resin F, commercial sample, 200 mesh.	45.0	45.0
7. Cation exchange resin A, hydrogen activated commercial sample, 200 mesh.	73.0	82.0
8. Cation exchange resin B, hydrogen activated commercial sample, 200 mesh.	73.0	87.0
9. Cation exchange resin C, hydrogen activated commercial sample, 200 mesh.	45.0	82.0
10. Cation exchange resin D, hydrogen activated commercial sample, 200 mesh.	73.0	82.0
11. Cation exchange resin E, hydrogen activated commercial sample, 200 mesh.	15.0	31.0
12. Cation exchange resin F, carboxylic acid type commercial sample, 200 mesh.	15.0	31.0
13. Cation exchange resin G, carboxylic acid type commercial sample, 200 mesh.	31.0	73.0
14. Cation exchange resin H, sodium activated commercial sample, 200 mesh.	39.0	73.0

TABLE II (cont'd.)

Adsorbent	% adsorbed using 0.1 gm. adsorbent per 100 cc. Trypsin sol. (8 mg./100 cc.)	% adsorbed using 0.4 gm. adsorbent per 100 cc. of same trypsin solution.
15. Cation exchange resin C, sodium activated commercial sample, 200 mesh.	none	73.0
16. Cation exchange resin I, sodium activated commercial sample, 200 mesh.	45.0	73.0
17. Colloidal magnesium aluminum silicate gel.	62.0 (conc.-1 cc./100 cc.)	82.0 (conc.-4 cc./100 cc.)
18. Synthetic magnesium silicate	82.0	89.0
19. Synthetic sodium aluminum silicate, 200 mesh.	82.0	87.0
20. High capacity synthetic sodium aluminum silicate, 200 mesh.	31.0	45.0
21. (Polyamine anion exchange (resin A 10% (Synthetic sodium aluminum (silicate 10% Suspended in colloidal magnesium aluminum silicate gel.	73.0 (conc.-1 cc./100 cc.)	>89.0 (conc.-4 cc./100 cc.)
22. Activated charcoal A	82.0	>89.0
23. Activated charcoal B	86.0	>89.0
24. Activated charcoal C	89.0	89.0
25. Activated Bauxite (Essentially Al_2O_3)	82.0	87.0
26. Fuller's Earth (Essentially SiO_2)	82.0	89.0
27. Diatomaceous earth	none	73.0
28. Kaolin (English)	73.0	82.0
29. Talc	45.0	89.0
30. Bentonite	73.0	82.0
31. Bauxite	73.0	82.0
32. Filtrol adsorbent	73.0	87.0
33. Aluminum hydroxide gel	73.0 (conc.-1 gm./100 cc.)	73.0 (conc.-4 gm./100 cc.)
34. Magnesium trisilicate	82.0	>89.0
35. Aluminum hydroxide powder	73.0	90.0

trypsin. In nature, trypsin inhibitors are known to occur in the seeds of leguminosae and other plants[6]. The presence of a specific trypsin inhibitor in pancreatic extracts has been demonstrated[7]. A brief summary of the many previous attempts to adsorb or inhibit trypsin is presented in Table I.

Experimental

The method used for the determination of tryptic activity was the U.S.P. method for casein digestive power[18] with a modification adapted from Gross's method[19]. This method is based upon the principle that faintly alkaline solutions of casein are precipitated upon the addition of a dilute acetic acid solution whereas its digestion products are not so precipitated.

Reagents:—

(1) Trypsin—Difco 1:250 (will digest approximately 250 times its weight of casein at 40° C. and pH 8.0 to 8.5).

(2) Casein—Difco isoelectric casein (1-2 per cent soluble in slightly alkaline solutions).

(3) Trypsin Solution—80 mg. Difco trypsin is dissolved in 1,000 cc. distilled water and pH adjusted to 8.8 to 8.5 with sodium carbonate (conc. = 80 γ/cc.).

(4) Casein Solution—2 gm. of Difco isoelectric casein is suspended in 600 cc. distilled water and 20 cc. N/10 sodium hydroxide is added with shaking. The mixture is placed in a water bath at 40° C. until casein is dissolved. The solution is then diluted to 1 liter and pH adjusted to 8.0 to 8.5. Chloroform is added as a preservative. Store in a refrigerator.

(5) Dilute acetic acid solution—1 cc. of glacial acetic acid is added to 9 cc. distilled water and 10 cc. of alcohol.

Method:—The adsorbent is added to the trypsin solution and the pH adjusted to 8.8 to 8.5 with HCl or Na_2CO_3. This mixture is shaken for 20 minutes and then centrifuged. A series of nine tubes is prepared each containing 5 cc. of the casein solution. Add to the series of tubes increasing amounts of the centrifuged trypsin solution, 0.55 cc., 0.65 cc., 0.8 cc., 0.9 cc., 1.0 cc., 2.0 cc., 3.0 cc., 4.0 cc., and 5.0 cc. Dilute each tube to 10 cc. with distilled water (pH 8.0 to 8.5) and place in a water bath at 40° C. for 1 hour. At the end of this time remove the tubes and acidify the contents of each tube with 3 drops of the dilute acetic acid solution. The tubes in which the casein is completely digested will remain clear when acidified while those which contain undigested casein will become more or less turbid under these conditions. Select the first tube in the series which exhibits no turbidity upon acidification, thus indicating complete digestion of the casein, and calculate the tryptic activity of the enzyme solution under examination.

Fifty-five one hundredths cc. of the trypsin solution as prepared digests 10 mg. of casein under the above conditions, a clear solution being obtained upon acidification with dilute acetic acid solution. This trypsin therefore digested 238 times its weight of casein. Five tenths cc. of trypsin solution (44 micrograms of trypsin) is therefore the minimum amount required to digest 10 mg. casein.

A blank is prepared for each adsorbent used by taking 10 cc. of the centrifuged trypsin solution and adding 3 drops of the dilute acetic acid solution. If the solution remains clear, it indicates no interference on the part of the adsorbent.

Calculations:—

$$\text{\% Tryptic activity} = \frac{\#\text{cc. of trypsin solution required to digest 10 mg. casein (.55 cc.) x 100}}{\#\text{cc. trypsin solution under examination required to digest 10 mg. casein.}}$$

The results that were obtained are listed in Table II.

Discussion

Logic indicates that agents used in the treatment of peptic ulcer should inhibit pepsin and adsorb or neutralize hydrochloric acid while permitting adequate protein digestion which means no inhibition of trypsin and the other intestinal proteolytic enzymes. A therapeutic index could be set up indicating the ratio between capacity to inhibit pepsin and capacity to inhibit trypsin. The ideal peptic ulcer therapeutic agent would almost completely inhibit pepsin and would not significantly inhibit trypsin. Into this category falls the anion exchange resin Type A almost to the exclusion of all others. Thus, aluminum compounds and magnesium trisilicate are excellent inhibitors of the activity of trypsin and pepsin.

A general intestinal adsorbent—one designed to treat diarrheas, etc., should not logically inactivate both pepsin of the stomach and trypsin of the intestine. If it did inhibit both, protein digestion would suffer. In the category of agents powerfully inhibiting both enzymes are found: aluminum hydroxide, magnesium trisilicate, charcoal, cation exchange resins, bentonite and kaolin. Thus, these agents have a point against them in their general application.

It is intended to extend these studies to cover the action of adsorptive agents on erepsin, lipase, amylase and other enzymes functioning in normal digestive processes. It is only with such information at hand that the physician can select the adsorptive agent which will be most suited to his needs.

Summary

Thirty-five different adsorbing agents which have been previously studied for their capacities to adsorb pepsin and endogenously produced toxic chemicals have been studied further for their capacities to adsorb trypsin.

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CORTICODIENCEPHALIC GASTROINTESTINAL SYNDROMES IN EPILEPTICS*

(Part IV)

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Diencephalic Neuroanatomy

Our attention to the mammillothalamic tract and particularly to the tuberal mammillary region was first attracted in 1938 (Weingrow, Fitch and Pigott 1938), when Pigott demonstrated the phenomenon of anteroposterior contraction at the base skulls of epileptics. He was then in charge of roentgenology at the New Jersey State Village for Epileptics. Although we concurred with him, we were more interested in the work of Henry Head on isolated neurological findings such as cortical sensory changes, evidences of single cranial nerve involvements, and isolated muscular atrophies than in x-ray of the skull. It was not until later when we had carried out pneumoencephalographic studies upon our epileptics in over 200 cases (Fitch, Pigott and Weingrow 1938) and had noticed dilation of the third ventricle that we began to realize the probable importance of the mammillary bodies and hypothalamus in relation to his phenomenon. As we proceeded with our studies of this region particularly with regard to the possible creation of supramesencephalic syndromes, we were more and more interested in the anatomy of the structures at the base of the brain particularly in those in the mammillary and adjacent region which we could visualize by our close study of the basal cisterns in our pneumoencephalograms. It was then that we familiarized ourselves with the work of Greving, Malone, Morgan, and Muskens on the mammillary bodies and adjacent structures.

The mammillary bodies are highly developed in many mammals. Their cellular constituent falls into a lateral and a medial as well as an external and internal mammillary nucleus. The small rostral end of the nucleus mammillary lateralis (nucleus prelateralis of Krieg) is small and consists of linearly arranged cells along the ventrolateral border of the hypothalamus.

The mammillary region is also important because of its situation in relation to the posterior perforated space of the mesencephalon. This area is located on pneumoencephalograms where it is found to be situated in front of the oculomotor nerve, and perforated by a great number of small vessels. Consequently that region is called the substantia perforata posterior. In front of this region are the

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mammillary bodies, the caudal ends of which mark the line between the mesencephalon and diencephalon. The aqueduct of Sylvius, extending forward through the mesencephalon, opens into the third ventricle at the diencephalon. In about 30 per cent of human thalami the third ventricle is obliterated in part in the posterior region by a junction, or rather a fusion, of the dorsal thalami of the two sides forming the commissura media. The cerebral peduncle occupies an increasingly larger part of the ventral field in passing from the lower to the higher mammals (Kappers, Huber and Crosby). The diencephalon shows a relatively greater increase in size in mammals than does the mesencephalon and its form and internal structure relationships show more marked variations.

Aside from the nuclei mentioned above as constituent of the mammillary body, the nucleus mammilloinfundibularis of Greving is important. Two nuclei were identified first by Malone (1914) as the nucleus mammilloinfundibularis or tuberomammillaris and the nucleus tuberus lateralis. The nucleus tuberomammillaris has cells that are comparable in structure to those of the nucleus supraopticus and the nucleus paraventricularis. The above two nuclei described by Greving and Malone are situated above the mammillary body and extend laterally on their way toward the mammillary bodies from the tuber cinereum. The rather extensive references to the workers who presented data on the preopticohypophyseal region in relation to water metabolism can be relevantly considered when dealing with the tuber cinereum. In the same way one might refer to the importance of the anatomy of the mammillary region because of the work of Beattie, Keller and D'Amour, etc. on gastrointestinal regulation by the last mentioned structure. The nucleus mammilloinfundibularis which forms what is known as Greving's frontotuberal path (Kappers, Huber, and Crosby) has a great many connections with various structures at the base of the brain, in front of the mammillary bodies, above them and behind them towards the region of the mesencephalon. The nucleus mammilloinfundibularis with other masses contribute fibres to the tractus hypothalamoreticularis of Greving which may pass caudalward to the mesencephalon and perhaps to even more caudal centers. The tuberal nucleus lateralis connects with contralateral thalamus through the tractus thalamoinfundibularis. The relationship of the above to the mammillary bodies is evident. The cellular structures of all these regions are therefore important. Greving (1922 and 1928) studied the cellular consistency of the mammillary bodies and found it to be comprised of a nucleus magnocellularis, a nucleus parvocellularis, and a nucleus mammillocinereus. The scattered gray at the side of the nucleus he termed the substantia reticularis hypothalamicus. The nucleus reticularis hypothalamicus lies between the structures which are believed to contribute to the tractus hypothalamicus reticularis of Greving (1928). Morgan (1928, 1930) believed that the nuclei of the tuber cinereum (described in the above connection with the mammillary bodies) are probably secretory centers for certain internal secretory glands, especially the thyroids and suprarenals. He believed that such centers might affect the metabolism, body temperature, blood pressure, heart rate, the motor function, the motor activity of the intestinal canal, pupillary control, states of consciousness, and other important functions. From the above we can see how important the

mammillary bodies really are even when independent of the anterior nucleus of the thalamus and the neurones above it.

Besides Greving, Malone, Morgan, and Muskens, other workers gave detailed attention to this region which has the following important areas around it: The zona incerta and field of Forel occupy the dorsal part of the subthalamic region. It is essentially a region of the passage of fibre bundles and has been recognized and studied as such. In this region is the peripeduncular region of Malone (1910), Morgan (1927), Papez (1929). This region, as do other hypothalamic areas, receives fibres from ansa lenticularis and is connected with the tectum by the incertotectal fibres and with the lateral geniculate nucleus [Gurdjian (1927), Beccari (1923), Huber and Crosby (1926)]. Here we remind the reader of our repeated cautioning with regard to the extreme functional importance of this area. We elaborated fully upon its regulation of gastrointestinal motor and secretory functions. The detailed references to this region in our account of hypothalamic regulation of water metabolism should also be remembered in connection with this anatomy. Bundles of this region join with those of striatal and subthalamic areas and receive collaterals of ascending lemnisci. Cajal (1911) and Dejerine (1901) traced fibres of the superior cerebellar peduncle, red nucleus, and reticular formation to the above.

The medial portion of the mammillary body is known to receive short internuclear fibres from the regions mentioned above [von Kolliker (1890), Dejerine (1901) and others]. The ansa lenticularis is an important structure in relation to the mammillary bodies and the hypothalamus. The structures of the zona incerta field of Forel and part of the subthalamus in relation to the mammillary bodies form an important sector of the cerebrum. Not only because they are known to be connected with the telencephalic basal ganglia, but also because collaterals of the internal capsule fibres were traced to this area in the rat by Gurdjian (1921) and Von Monakow (1905), believed that in man there are bundles from the temporal lobe, the operculum and other parts of the island of Reil which connect with the zona incerta. One can readily see how such connections involved almost every portion of the cerebrum. If this is so, then anything can be expected in the form of symptoms in an epileptic individual whose pneumoencephalogram shows a definite dilation of the third ventricle thus compressing some of these structures. We have seen many such dilations in the course of pneumoencephalograms of over 500 epileptics during the past ten years. Not only is the third ventricle dilated in most of our cases, even in those who showed very little evidence of pathology in the other ventricles, but we invariably found dilation of the basal cisterns and particularly the cisterna pontis. This might account for involvement of hypothalamic and mammillary regions particularly if the aqueduct was also markedly dilated as occurred in some of our cases. These findings show the parallelism between a basilar external hydrocephalus and an internal one. Both of the above are probably the result of pathology within the brain structures elaborated upon above.

In our pneumoencephalographic findings (Fitch, Pigott, and Weingrow 1938) we invariably encountered dilations of the cisternae at the base of the brain and

saw evidences of dilation particularly of the cisterna pontis and the cisterna ambiens. With these we noted evidences of pressure against the retrothalamic and the hypothalamic, as well as the tuberomammillary region. We were not surprised that Morgan (1928, 1930a) regarded the nucleus tuberomammillaris as being a center affecting the thyroid gland and the substantia grisea as probably related to the functional activity of the suprarenals. Neither were we surprised when we found that the nucleus mammilloinfundibularis, particularly the frontotuberal part of Greving, was considered by various authorities particularly Aschner (1912), and Camus and Roussy (1913) as a center regulating water and salt content of the body and that Cushing (1912), Bailey and Bremer (1921), as well as Smith (1927), regarded this region as being responsible for the production of polyuria. In addition to the above it may be noted that Greving regarded the nucleus supraopticus rather than the nucleus tuberis as responsible for the production of glycosuria. This region, in other words Greving's frontotuberal path, mamilloinfundibular region was also considered as containing centers, in the neighborhood of the nucleus subthalamicus for the regulation of the size of the pupil (Karplus and Kreidl 1913). Greving (1922a and 1928) as well as Karplus and Kreidl (1918), regarded this region as controlling contractions of the urinary bladder. At this point the reader should be reminded that it was the pioneer work on the hypothalamic structures by Karplus and Kreidl that resulted in the wave of enthusiasm and in turn in the remarkable findings of Beattie and his followers. It was the work of Karplus and Kreidl that invited the modern data on water metabolism as noted in the material of Fink, Ranson and Magoun etc.

The mammilloinfundibular region was also regarded by Greving (1928), and others as acting on intestinal muscles. The region above the mammillary bodies is of great importance not only because of its control of visceral actions but also because of its regulation of motor manifestations of emotional reactions. Whether such are connected with the preparoxysmal cry of the epileptic and his outbursts of rage remains to be determined. It is this supramammillary region or that region located in the caudal and central part of the diencephalon which is regarded by Bard (1928 and 1929), as the center concerned with sham rage and hence with feeling tone.

It might be well to digress at this point so that we may discuss the hypothalamus in relation to the mammillary body. In this way, we feel that the connections between both structures will strengthen our conception of the mammillothalamic tract and the fact that this tract is not an isolated one, but is connected not only with the hypothalamus, but also with the telencephalic ganglia. The mammillary bodies will thus be conceived of as reaching the anterior nucleus of the thalamus from a medial and inferosuperior direction. The hypothalamus consists in mammals of the olfactory commissural portion, that is the pars optica hypothalami which contains the optic chiasm, and the supraoptic commissure. It also consists of a glandular portion to the hypophysis. A certain olfactovisceral correlation center which may be termed collectively either the hypothalamic nuclei or the tuber cinereum and mammillary bodies are situated in this vicinity. From

the above we can readily understand that certain nuclei such as the nucleus mammilloinfundibularis of Malone is directly related to the above very important structure. It is therefore not surprising to find that certain tracts such as the ansa lenticularis fibres which start accumulating in the ventrolenticular nucleus and pass medially to the inferior thalamic peduncle and then pass into the diencephalon at the ventral border of the peduncle finally giving off fibres to the mammilloinfundibular region (Morgan 1927 and Malone 1909) should be related to the above. These fibres, mentioned above, when they enter the mammilloinfundibular region specifically are directed to the nucleus of Malone (1909). It is therefore important that besides showing the relationship between the hypothalamus and the mammilloinfundibular nucleus that we trace the fibres of the ansa lenticularis further and see how they connect with other structures in the region of mammil-

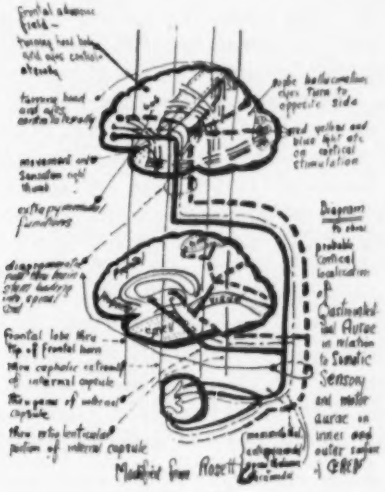

Fig. 11

lary bodies. We find that fibres of the ansa lenticularis have been carried across the supramammillary commissure through the subthalamic nucleus. Many fascicles (Morgan 1927), swing to the field of Forel combining with the cells of Forel H2. These fascicles which are directed down through the supramammillary commissure distribute fibres to the nucleus of the field of Forel, to the zona incerta and to the capsule of the red nucleus (Wilson 1914), and finally to the nucleus interstitialis of the medial longitudinal fasciculus and the posterior commissure. In discussing the mammillary bodies in relation to the gastrointestinal regulating role Tilney and Riley mention some of the above structures at the base of the brain and then direct attention to fibres which end in the corpora quadrigemina. In view of all the experimental data which we described in detail we feel the above rather inadequate and very limited. The information concerning so large a tract

as the gastrointestinal nerve structures governing such an old system should be much more extensive.

The relation of the field of Forel to the lenticular nucleus was recognized by Forel (1877), Probst (1906), Von Monakow (1895), Edinger and Fisher (1913), Wilson (1914), Riese (1924b), and finally Kodama (1929). Since we have shown that the ansa lenticularis eventually connects with the mammilloinfundibular region and therefore with the mammillothalamic tract eventually, it seems that the telencephalic basal ganglia cannot altogether be separated from the mammillothalamic region. It is known that this field of Forel does connect, by means of well traced fibres, with the lenticular nucleus. The part of the lenticular nucleus which is responsible for and connects with the infundibular nucleus of Malone was said by some authorities to be the putamen and by others the globus pallidus. Kappers, Huber and Crosby state that the origin of the fibres mentioned above was believed to be in the putamen by some authorities such as Edinger and Fisher (1913), Tarasewitsch (1902), and Von Monakow (1895 and 1910). Kodama (1929), believed however that the fibres originated in the globus pallidus. The termination of the ansa lenticularis, which, as has been shown above, is connected with the mammilloinfundibular nucleus of Malone, is believed to eventually be in the red nucleus by the way of unmedullated fibres. This view is held by such investigators as Sachs (1909), Economo (1918), Riese (1924b), and Kleist (1918). The above connections with eventual termination in the posterior commissure was also agreed upon by Pollock (1922), Kodama (1929), Rioch (1929), C. & O. Vogt (1920), Morgan (1927), Muskens (1914 and 1922). While most of the authorities carried fibres from the above structures to the nucleus interstitialis, Jacob (1923 and 1925) carried the same fibres to the nucleus of Darkschewitsch. Connection with the last mentioned structures thus definitely establishes a neural chain of a distinct autonomic character. This gives additional anatomical support to the work stressed by Donal Sheehan on the regulation of gastrointestinal function and to that emphasized by Hare on the control of water metabolism.

In order that the reader might take all this anatomical material dealing with the mammillothalamic tract, particularly the portion of the mammilloinfundibular region, into serious consideration, we refer him to some of the neurological findings which we made (Fitch, Pigott, and Weingrow 1938). In the six facial photograph figures which we present there are evidences of cranial nerve involvement. When we were repeatedly impressed with the fact that a patient may have generalized convulsions and nothing more than involvement of extraocular musculatures, facial, pupillary changes, as well as involvement of the tongue, we felt that such an isolated neurological syndrome could be possible in the presence of the dilation of the third ventricle particularly if such is accompanied by a dilation of the cisterna pontis and interpeduncularis as well as the cisterna ambiens. We never felt that such involvement, if merely peripheral, could be accompanied by convulsions and be directly connected with a lesion which is situated only out of the brain. On the contrary we were repeatedly impressed by the fact that such involvements of isolated cranial nerves could be really cortical in various lobes of the

brain and caused by an inflammatory process with subsequent nerve degeneration. Eventually such a process, although producing evidence of isolated focal involvements, could also be responsible for a dilation of the third ventricle. It should be emphasized that this should be rather common since a large part of the final common pathway consists of long neurones. The collaterals of these have been shown, in the anatomical descriptions above, to connect with structures in the vicinity of the third ventricle. We were therefore convinced that some of our anatomical structures, although seemingly hypothalamic in particular and diencephalic in general, were mostly cortical in origin. We see, therefore, that the mammillary bodies and the subthalamic regions might be connected with and in fact be in close relation to the cerebral cortex. This has been shown by various authorities such as Foix and Nicolesco (1925), Von Monakow, and Dejerine. Other authorities felt that such connections might be indirect. Such connections exclude of course the upper components of the mammillothalamic tract. It is known for instance that the striatum connects with the cerebral cortex and that the nucleus subthalamicus connects with the striatum by the way of the ansa lenticularis and through the area of Forel. This has been shown by Dejerine (1901), Von Monakow (1895) and (1905), Ramon y Cajal (1911), Tsai (1925), Foix and Nicolesco (1925), Papez (1929), and finally Rioch (1929a). Connections with the cerebral cortex were denied by Winkler and Potter in the rabbit and cat (1911 and 1914).

As we went along with the performance of pneumoencephalograms we were convinced that a dilated ventricle in either of the cerebral hemispheres, that is an appreciable dilation of the body of the lateral ventricle could, if large enough, produce pressure upon the thalamus and indirectly affect fibres which eventually connect with the mammillothalamic tract. That such could be the case can be seen from the figures which we presented (Fitch, Pigott, and Weingrow 1938). That this could also occur through the involvement of the anterior nucleus thalamus is self evident. Dilation of the third ventricle would exert pressure upon the thalamus and a marked dilation of the body of the lateral ventricle could easily press upon the anterior nucleus of the thalamus. This is partly true with a dilation of the frontal horn of the lateral ventricle. We are, however, not so much interested in the thalamus proper as in the subthalamic, mammilloinfundibular region as related to the ansa lenticularis structures and eventually the structures below this, such as the substantia nigra and the red nucleus which will definitely be affected by marked dilation of the third ventricle and deformities of the aqueduct of Sylvius. This the reader can easily be convinced of by referring to the figures in the reference cited. Kappers, Huber and Crosby have shown that the mammillary bodies are connected with the nucleus subthalamicus and by their indirect connection with ansa lenticularis and other structures finally form synaptic contact with fibres which descend to the red nucleus of the opposite side after decussating in the mammillary commissure on their way to red nucleus of the same side. This has been shown by Von Kolliker (1896). That fibres from the contralateral subthalamic nucleus may be traced to the red nucleus of the same

side has been shown by Foix and Nicolesco (1925), and Gerdjian (1927). The last mentioned authority connected fibres from the above to the substantia nigra. This was confirmed by Rioch (1929a). The region mentioned above was also said to contain homolateral and contralateral fibres from the hemisphere connected with the optic tract system. This was shown by Bochenek (1908) and later verified by Loepp (1912), and finally confirmed by Tsai (1925). We have repeatedly seen dilation of the third ventricle as well as that of the aqueduct of Sylvius not only in patients suffering from hemiplegia connected with convulsions, but also in individuals who showed scattered neurological findings such as cranial nerve involvement and atrophy of small muscles. The neglect of the diencephalon by the clinical neurologist, who has developed definite syndrome entities in the brain stem, is due to the fact that one does not see such definite clinical entities as hemiplegia in the diseases of the former as in diseases of the latter. This gives the clinician the false impression that other functions such as the modification of sensory impressions, trophic and other functions are unaffected by lesions in the region of the diencephalon. The sooner this tendency is overcome and advantage is taken of the many connections of the diencephalon the quicker will the problem of the relation between the somatic and vegetative be understood.

In the above presentation of the literature we tried to impress the reader with the fact that the mammillary bodies are not just isolated structures but that they connect intimately with not only the supraopticohypophyseal system in front, the subthalamic region above, but especially with the fibre tracts that are directed from the basal ganglia to the field of Forel and the subthalamus. These mammillary bodies form a link with many parts of the cerebrum and eventually connect with the mesencephalon and other parts of the brain stem, and finally end in various columns of the spinal cord. Although in the above pages we occasionally digress to the description of the ansa lenticularis and the telencephalic basal ganglia most of the facts which we presented and our immediate concern is with the mammillary bodies, the supramammillary region, the mammillary commissure, and the infundibular region. The special regions described above are situated in direct relation to the mammillary body. They are therefore specifically connected with the function of the mammillothalamic or thalamomammillary tract which is a definite fibre path that stretches downward from the anterior nucleus of the thalamus passing various structures and eventually running parallel with various fibre tracts which, though not as compact and distinct as those of the thalamomammillary are nevertheless definite and extend forward into the supraoptic and other regions in front of the mammillary body as far as the anterior commissure. It should be remembered that the fibres of the mammillothalamic tract run diagonally across the original figure which we described as the body of the basket or the anatomical polyhedron. The mammillothalamic tract while stretching through the region described above can therefore be affected not only by a dilation, shape, change, or shifting of the third ventricle but also because the anterior nucleus of the thalamus is so situated that the bodies of the lateral ventricle when dilated or shifted can impinge upon it. We can therefore

Fig. 12—Top left, Fig. 13—Top center, Fig. 14—Top right, Fig. 15—Bottom left, Fig. 16—Bottom center, Fig. 17—Bottom right.

expect involvement of this tract from above directly by pressure upon the anterior thalamic nucleus. In the data which we presented above, therefore, we did not intend to be pedantic and burden the reader with a great deal of material from the literature. We did object however to the anatomic limitation which this region was presented as having in the diagram of Beattie as analyzed by Donal Sheehan. In that diagram, if the reader recalls, the area at the base of the diencephalon was divided for the purpose of illustration of neurogenic (suprasegmental cerebral preganglionic) control of gastrointestinal and urinary function into a preoptic, tuberal, and finally a mammillary region. Such limitations as the reader can very well see are not in accordance with the findings as shown by the neuroanatomic investigators whose results we have presented above.

For the functional junction of the mammillothalamic tract with the other basal structures concerned with gastrointestinal, urinary, and other autonomic function we favor the scheme presented by Kappers and Crosby. In that scheme the mammillothalamic tract is seen to run parallel with the preoptic components of the stria terminalis, the fibres from the periventricular gray, as well as the fibres of the dorsal supraoptic commissure. In such a relationship many structures from the floor of the diencephalon and some coming from telencephalic regions are found to be intimately connected with the fibre pathways mentioned above that run parallel to the mammillothalamic tract. Among the structures that are in this way connected with the mammillothalamic tract may be mentioned, the lateral preoptic area, the medial preoptic area, the prethalamic nucleus, the fornix, the anterior commissure, amygdaloid nucleus, the medial forebrain bundle, the pyriform lobe and its preoptic connection, the periventricular gray, the supracommissural components of the stria terminalis, the lateral hypothalamic nucleus, the tangential nucleus, the ventromedial hypothalamic nucleus, the dorsal longitudinal fasciculus (of Schutz), the mammillotegmental fibres, the dorsal premammillary nucleus and other nuclei as well as some other fibre bundles. If the reader can visualize such connections with the mammillothalamic tract he will realize the purpose of our presentation of a bird's-eye view scheme of the vegetative neurogenic components that are responsible for the control of gastrointestinal and urinary function which we presented in the form of a basket, the floor of which consists largely of the structures which we claim to be connected with the mammillothalamic, such structures forming the floor of the body of the basket. Once the reader has visualized a scheme such as the above and has mentally connected it with the hypothalamic structures as presented in the literature dealing with the area of Forel, with the ansa lenticularis, and with the other structures connected with the ansa lenticularis above and below these in turn; once he has done the same with the mesencephalic region he will appreciate that such an arrangement is a very serviceable scheme for the neurologist. In many of the cases of focal epilepsy we can prove by the following that the regions described above can easily be affected by a lesion which involves pyramidal systems and produces a hemiplegia. Although this starts in the cortex of one side of the cerebrum, by means of descending degeneration, it can involve this entire mammillothalamic or the corticothalamomammillary tract and adjacent regions

and then be responsible for gastrointestinal and urinary phenomena that accompany the fit thus resulting from the pathologic process higher up.

In the course of our presentation of cases we will show that a patient who has suffered a paralysis of one side of the body because of a cerebral embolism, a cerebral hemorrhage, a localized inflammatory or traumatic lesion of the cerebrum, might eventually present a paralysis of the body which is partial or residual and suffer from focal Jacksonian epilepsy. A focal lesion does not necessarily have to be cortical or subcortical, it can even be deeper down so that its consequent degeneration may involve the areas which we described anatomically in detail. There is thus no reason why we should have definite pathways for the localization of hemitremor, hemichorea, hemiathetosis, hemidystonia, hemiataxia, etc., and have none for a hemiconvulsion which is really a toniclonic Jacksonian phenomenon. We see no reason why dystonia, chorea, and myoclonia are more important than a combination of tonus and clonus such as we see in Jacksonian fits. If we accept a definite pathway for a Jacksonian convulsion, we will realize that in the descending degeneration of the fibres there were pathologic changes which were responsible for the production of a convulsion of half of the body. These cannot eventually, by connections of an anatomic nature such as we have described in the literature heretofore, become a generalized convulsion. This as everyone knows is a common occurrence among many cases which start as focal epilepsy and eventually become generalized. If the degeneration runs through the the areas at the base of the brain, particularly those connected with the neurogenic control of gastrointestinal and urinary functions, we have a scheme such as we will eventually describe in our material and which fulfills most of the symptoms and clinical findings of the common seizure.

If the neurologist and neurosurgeon will follow along the findings laboriously given to them by the neuroanatomists they will be able to utilize a great deal of the material seen in epileptics to help them not only with the exact localization of cortical, subcortical, and diencephalic lesions but eventually to take advantage of so many of the vegetative disturbances not only of the gastrointestinal and urinary tract, but also of the cardiovascular and other systems, as well. There are many other vegetative symptoms particularly sweating manifestations of autonomic origin which they see so often and which have been for so long step children as far as their exact cortical and subcortical localization within the cerebrum is concerned.

That a toniclonic or Jacksonian and other forms of focal epilepsy can actually be mapped out has been shown by the extensive work of Penfield, Foerster, the Vogts, and very many others because of foci which they have assigned function to in various lobes of the brain particularly in the orbitofrontal, in area 6ab, in area 5b, in area 13, and finally in some portions of the temporal lobe. Such foci of irritation show definitely that we can have tonic but that there are mostly clonic disturbances within the cerebral cortex and below the same. Whether a clonic reaction is merely an intermittent interruption of a tonic reaction, we cannot definitely state. We do know however that the diencephalon is regarded by many

authorities as the center of tonus. This has definitely been proven by Magnus (1925), Ranson and Hinsey (1929), Rademaker (1926), Windle (1929), Weed (1914), Sherrington (1906), and others. It is evident that this localization of tonus might add tonus in smooth muscle to the controlling influence of the diencephalon. This being the case another impetus is given to the work started by Beattie and continued by Sheehan, Keller and others. It would also tend to support the view that cortical impulses of tonus traveling to the intestines might favor the mammillothalamic path via the anterior nucleus.

When the above anatomical and clinical data are seriously considered one can definitely visualize that the diencephalon might contain small initial lesions, or foci of degeneration which started as larger lesions elsewhere and eventually remained as residuals and that such lesions were responsible for the findings in the eye musculature, the atrophy of the tongue, the facial and lingual paralyses, and the invariably present pupillary disturbances which we presented in the figures of a previous paper (Fitch, Pigott and Weingrow, 1938). That fibres controlling these extend upward from the mesencephalic and other brain stem nuclei into the diencephalon will be shown later. The centers for such facial musculature will also be shown to be extending downward from the frontal cerebral cortex. That centers for the contraction and dilation of the pupils are located not only in the mammillothalamic but also in other diencephalic structures particularly at the floor of the diencephalon has been shown above.

A further description of the subthalamic nucleus of Winkler and Potter (1911 and 1914) may be seen from the literature on this nucleus. In man this nucleus lies lateral to the tip of the substantia nigra. It has large cells with coarse granulations. It was known by earlier workers as corpus luysii. This nucleus subthalamicus falls within the zona incerta of most observers. A center for dilation of the pupil has been described in the forefrontal and medial portion of the nucleus subthalamicus by Karplus and Kreidl (1909), Spiegel (1928), Greving (1928), Ingram, Ranson and Hannett (1931). No wonder that the pupillary reflex has such extensive representation. Its localization in the cortex of almost every lobe demands a widespread representation at the base of the brain from which the fibres responsibile for this reflex reaction must radiate on their way to the cortex. Some of the authorities mentioned above obtained such dilations from various other portions of the brain stem as well as this center. Here it might be well to mention the fact that pupillary changes may be noted in various portions of the diencephalon, not only in the structures lying in relation to the mammillothalamic tract, the hypothalamus and subthalamus, but also even within the thalamus itself. Stavraky in his very extensive and illuminating paper dealing with stimulation of the interpeduncular nucleus also shows that the optic thalamus, when stimulated, serves as a center of parasympathetic activity and is related to pupillary dilation. Such a broad diencephalic source of reaction is necessary because the pupil is represented throughout the lobes of the cortex.

In the following presentation of the literature as a continuation of the subject of mammillothalamic tracts, that is, mainly in the lower or mammillary por-

tion, we will attempt to show that not only is this mammillothalamic tract connected with many structures in front and in the direction previously outlined, but also that there is a definite mammillohypothalamic tract. This will be elaborated upon because it is imperative that the structures mentioned be traced directly into the substance of the spinal cord. Those structures from the brain stem particularly the cranial nerves which form and connect with the parasympathetic controlling gastrointestinal action will be emphasized. Furthermore, the mammillothalamic tract system will be shown to be connected intimately at the point of its entry into the mesencephalon, not only with the posterior commissure, but also with a collicular commissure and that it is intimately bound with a great network of commissural and decussational fibre systems that extends from the posterior wall of the body of the basket; that is the retrodiencephalic area and encompasses and intimately connects with the epithalamic regions and finally becomes fused with almost every fibre tract that extends from the cortex of almost every cerebral lobe such as the frontopontine, parietotemporooccipitopontine, lateral and medial corticobulbar, etc., and eventually this mammillothalamic system becomes continuous with the medial longitudinal fasciculus. Besides having vegetative functions, this network becomes connected with cranial nerve function involved in eye and head movements. In uniting as above with the medial longitudinal fasciculus, the mammillothalamic system may be said among other connections to become part of the tract described by Muskens and formed by a combination of the two interstitial nuclei, the nucleus of Darkschewitsch, the fibres from which finally descend and end in the spinal cord as the lateral ground bundle.

Kappers, Huber and Crosby, in their analysis of the relation of the mammillary region, particularly the pars lateralis in mammals, discussed the terminology involved in the various nuclei of the mammillary region. They mentioned the dorsal premammillary nucleus of the rodent which is formed in relation to the lateral thalamic nucleus and the latter with medial hypothalamic areas. They state that Rioch (1929) applied to the dorsal premammillary nucleus the name of supramammillary nucleus and that Papez (1932), and Chu (1932), used this terminology applied by Rioch (1929). Lateral to the nucleus hypothalamicus posterior (which is continuous with the periventricular gray of the tegmentum) is a mammillohypothalamic tract and the lateral hypothalamic nucleus. Though seemingly irrelevant, it might be important that Kappers, Huber, and Crosby mentioned in the above connection that from the dorsal nuclei of the tegmentum stretching even beyond the mesencephalon probably into the mammillary region and eventually connecting with the dorsal longitudinal fasciculus are fibres which eventually connect with the motor nucleus of the vagus nerve. This definitely shows, therefore, that we have not only sympathetic but also parasympathetic fibre systems in the great network connected with the mammillothalamic and mammillohypothalamic tract.

At this point it is well to remind the reader that in our work not only on cases such as we are dealing with in this subject, but in epilepsy in general we

have, during the past decade, encountered many patients who presented dilations of the third ventricle and not infrequently dilations of the aqueduct of Sylvius. This may be seen in illustrations #19 and 20 on p. 164 of our previous publication. (Weingrow, Fitch, and Pigott, 1941). We can, therefore, never say enough in trying to bring home the point that the occurrence of isolated paralysis or atrophies of facial, neck, and eye, tongue and pharyngeal muscles are important because of the relationship of the nerves controlling them at their nuclear locations to the mammillothalamic parasympathetic and related tracts controlling vegetative functions. Far be it from us to propose new sets of syndromes in which isolated items such as scattered sensory disturbances, partial muscular atrophies (Wartenberg) isolated tendon reflexes and single or multiple cranial nerves indicate cerebral noncapsular involvement. These have been stressed in epilepsy, generations back by Brown-Sequard, Oppenheim, and Muskens. In nonepileptics these syndromes have been proposed in a too much neglected two volume work by Henry Head. In presenting data on the relationship between the fibres direct from the mammillothalamic tract towards the mesencephalon to the posterior commissure, Kappers, Huber, and Crosby, state that the lower end of the medulla oblongata is reached behind the level of the sensory decussation, the medial longitudinal fasciculus with its associated medial tectospinal and probably the ventral spinothalamic that overlie the pyramid. The above connections of the medial longitudinal fasciculus are traced from the subthalamic region and shown to be located in the neighborhood of the aqueduct of Sylvius near the midline. The above gives additional strength to the statement that the spinothalamic tract has a wide fibre scope.

The mammillothalamic and mammillohypothalamic tract by their eventual junction in the mesencephalon with the posterior commissure and the medial longitudinal fasciculus, will become more important when it is realized that some of the fibres are continuations of the motor nuclei of the cranial nerves within the brain stem. The medial longitudinal fasciculus interrelates eye muscle nuclei with contralateral and homolateral vestibular nuclei. It contains fibres from the contralateral and homolateral nuclei of the posterior commissure. Those from the homolateral nucleus of posterior commissure constitute the nucleofascicular chain of Muskens. Therefore, the homolateral interstitial nucleus of the medial longitudinal fasciculus constitutes the fasciculus interstitiomesencephalospinalis of Muskens. Those bundles described above have been seen by Held (1893), Boyce (1894), Redlich (1899), Van Gehuchten (1904), Probst (1900a), Karplus and Economo (1909), Economo (1911), Ramon y Cajal (1911), and Muskens (1914, 1922 and 1930). The modern advances in electroencephalography with its particular stressing of the fact that carbon dioxide, glucose, acids and bases cause changes in wave frequencies demand that more be known with regard to cerebral localization of the autonomic. Although somatic fibres within the cerebral hemispheres could be the carriers of impulses, the chemical effect upon which might be responsible for frequency changes, it must be conceded that metabolites are more related to autonomic fibres.

Fig. 18—Top left, Fig. 19—Top center, Fig. 20—Top right, Fig. 21—Bottom left, Fig. 22—Bottom center, Fig. 23—Bottom right.

In the region where the mammillothalamic fibres descend to join the tegmentum at the level of the posterior commissure, there are other interesting structures as shown by Kappers, Huber and Crosby. They state: "The superior colliculag commissure interconnects the tectal areas of the two sides and carries a number of crossed fasciculi of efferent tracts such as the tectospinal. The superior colliculus is a way station in the visual reflex path in the region. They may be modified by other reflex afferent impulses and serve as an efferent center for other types of reflexes."

The reader knows however of the importance of the tracts to gastrointestinal, urinary, and other autonomic functions. He may not, be definitely impressed with the fact that there are ascending and descending autonomic tracts within this bundle. Further reference will convince him of their existence. In other words, instead of repeatedly using the term mammillothalamic, we might as well use thalamomammillary. We also could have traced this nucleofascicular tract directly into the frontal cortex. Then we would have been repeating the term corticothalamomammillary tract. We also might have used the term mammillothalamocortical. No matter how many references to the literature we might have presented, the reader would still be convinced of the fact that our adherence to the subject under consideration, namely the neurogenic control of the gastrointestinal and urinary functions is effected by an elaborate structure.

When the reader notices however that instead of adhering to this tract we repeatedly refer to the phenomena of eye and head movements, he begins to wonder whether we are not straying from the subject. Reference to the work of Watts and Fulton shows that the precentral, prefrontal, and other areas that are directly connected with the cortical representation of the extrapyramidal tract contain fibres that are intimately associated with the autonomic control of gastrointestinal and urinary functions. That being the case, and particularly since tongue movements, rhythmic chewing and swallowing, eye movement, head and neck movement, are intimately associated with the above localizations we cannot but look upon such functions as adjuvants to alimentation. We have repeated that the head, eye, neck, and body movements localized within are as such as 6a, b, 5b, and 13, are in the course of a convulsion associated with dilation and contraction of the pupil. The two last mentioned functions are definitely sympathetic and parasympathetic, as the reader knows. Their relationship to gastrointestinal functions becomes, therefore, self evident. For the above reason, in our work during the past decade, we have repeatedly referred to the areas of Penfield, Foerster, the Vogts, and many others (Weingrow, Fitch, and Pigott 1941). Although we were constantly perplexed by the existence in the areas mentioned above of hemicorporal movements, eye movements, head and neck movements, we always noted their association to sympathetic and parasympathetic function. As time went on we invariably felt that in the Jacksonian fit associated with these areas in the course of the fit reaction, there were certain characteristics pointing towards activity by the sympathetic and parasympathetic in the course of the pupillary dilations and contractions that occurred during these seizures. We

invariably felt, however, that some day a clinician who has had the experience with these reactions would associate them with activity in the pyramidal, corticobulbar, parietotemporopontine tracts which eventually connect by internuncials with other parts of the brain stem. We furthermore knew that these tracts are alleged by many authorities to contain descending sympathetic and parasympathetic fibres. At this point we feel that both the anatomist and clinician might take exception to our statements. If they do, let them remember that an argumentative discourse on the subject of the neurology of epilepsy in an era when such clinical neurology has been almost totally abandoned for the experimental would be rather stimulating. Far be it from us to claim such originality. We are merely stating it in different language than Muskens who cited Brown-Sequard, Oppenheim and many others.

Although we know of the fondness of Muskens for the olivospinal tract and of his great work as a pioneer in the posterior or medial longitudinal fasciculus and particularly of his experiments on myoclonus in relation to the above structures, and particularly of his interest in eye movements, we never conceived that he would connect eye, head, and body movements even on a basis of circus movement explanations to the telencephalic basal ganglia. It is however seen that he favors this in the following quotation taken from Kappers, Huber and Crosby: "The posterior longitudinal fasciculus contains bundles which interconnect eye muscle nuclei with the accessory nucleus and motor nuclei of cervical spinal cord. Reticulospinal fibres which descend from reticulotegmental gray to the cord (Von Monakow, 1895, Kohnstamm and Quensel, 1908, Van Gehuchten, 1904, Probst, 1902a, Papez, 1926, etc.) contain fibres connected with oculomotor, and facial nuclei. Fibres from the superior vestibular to the superior longitudinal fasciculus form important pathways that connect with the area of Forel. Muskens, (1932) showed that injury to the globus pallidus gives conjugate deviations of the eyes to the injured side. Ascending fibres from the commissural (posterior) nuclei to the striatum (globus pallidus) produce the above. The globus pallidus also derives fibres from other commissural nuclei. Injury to the oral end of the globus pallidus is lateral conjugate deviation of head and eyes to the injured side with circus movements which persist. We know that Muskens was probably intrigued by the fact that his findings on eye movements connected with the striatum. Being particularly famous for his development of the relation between the posterior commissure and various brain stem tracts controlling head and neck movements instead of being drawn to the areas within the cortex concerned with head, neck, and eye movements during a fit, he was drawn to the oculogyric phenomena seen in diseases of the tegmental basal ganglia. Eventually the clinical phenomena of seizures will be related to the electroencephalographic phenomena. Whether such relationships will prove or disprove the theories of Muskens on myoclonic charges remains to be seen. That there is some such parallelism between the clinical and bioelectric may be seen from the fact that a transient impairment of consciousness accompanied by a rhythmic three per second twitching of the facial muscles is invariably accompanied by a discharge of waves and spikes, the complex occurring at a frequency of three per second. With data such as the above

and a parallel march of autonomic manifestations of the petit mal attack references to the anatomy of the autonomic are never superfluous.

It is rather interesting to note that certain pioneers in the field of striatal syndromes disagreed with Muskens as to the localization of head and eye movements. This they did after a thorough analysis of the literature (Davison, Goodhart, 1931). Their agreement with us in giving the movement a pyramidal rather than an extrapyramidal localization was on the basis of analysis in the work not only of the Vogts, but many others. They showed that not only in epilepsy but also in other conditions, head and eye movements as well as paralysis of half of the body may be localized in a number of areas in the cortex. This proves the point of multicortical hemicorporal motor localization of part of the body. Whether Muskens and Goodhart are partially correct is unimportant. The crucial facts are that with either type of eye-movement disturbance there is invariably a certain amount of sympathetic as well as parasympathetic imbalance. This is seen in encephalitis of the brain stem as well as in epileptic conjugate deviation.

Davison and Goodhart start by stating that the present knowledge concerning the anatomy of the oculogyric spasm and paralysis owes much to the work of Dejerine (1926 and 1895) and of Tilney and Riley (1921). They further state that the cephalogyric and oculogyric centers can be considered in two main divisions. The centers which they gave above were the cortical and intermediary or supranuclear centers. We will dispense with an elaborate analysis of the situation by merely citing from the work of Davison and Goodhart and let the reader draw his own conclusions. After this citation we will give a summary taken from the work of these authors to show what we have attempted to prove in the past ten years in support of Rosett, namely, that the intercortical systems are concerned with eye movement and therefore with a multicortical representation of the autonomic (Weingrow, Fitch, and Pigott, 1941). "The right cortex turns the eyes to the left and the left cortex turns the eyes to the right. As Grasset (1879) has shown each hemisphere sees and looks through the opposite side. This can be emphasized further by stating that acoustic, equivilatory and sensory impressions bring reflexes to one or two of the coordinating centers" (Davison and Goodhart). The second quotation from Davison and Goodhart (1931) follows: "Foville in 1859 mentioned clinical paralysis of associated movements of the eye to the left in a case of left facial palsy and right hemiplegia. Prevost (1868), experimenting on dogs by producing lesions of the corpus striatum and thalamus, induced conjugate deviations of the head and eyes." Another quotation from Davison and Goodhart follows: "Ferrier (1879 and 1886) on stimulating the base of the first frontal and part of the second frontal convolutions of the brain of monkeys, induced elevation of the eyelids, dilation of the pupil, and conjugate deviation of the eyes, and turning of the head to the opposite side. Later he obtained somewhat similar results by stimulating the angular gyrus and the temporosphenoidal convolutions." The next quotation also shows results obtained during involvement of the parietal region. "Landouzy (1879) following the experiments of Hitzig and Ferrier, thought that these lesions were located in the right frontoparietal region and differentiated between paralytic and irritative

lesions." Here we see a parallelism between eye position and pupillary reactions. We cited many references dealing with the latter which resulted from hypothalamic stimulation in our descriptions of the mammillothalamic pathway.

The following quotations cover not only the frontal and parietal, but also the occipital lobes. They also involve not only experimental but clinical material such as brain tumor. The quotation taken from Davison and Goodhart will be given without interruption, "Wernicke (1889 and 1903) and Henschen (1910), placed lesions in the inferior parietal and supramarginal gyrus. Horsley and Schäfer (1888), and Beevor and Horsley (1888 and 1890), agreed with the observation of Ferrier, (1886).

"Mills (1879 and 1881) during an operation for a brain tumor, by stimulating the posterior part of the second frontal convolution induced complete deviation of the head and eyes to the opposite side. Conjugate deviations of the head and eyes were observed by the same author in a case of tumor of the pons.

"Schaffer (1904) described a case of cerebral syphilis with a severe lesion of the right frontal lobe and paralysis of associated movement of the eyeballs to the left.

"Mott and Schäffer (1890), by stimulation of the middle portion of the foot of the second frontal convolution, demonstrated lateral movements of the eyeballs.

"Grünbaum and Sherrington (1902 and 1912), and Sherrington (1911) were the first to use unipolar faradization. The inferior and middle frontal convolutions caused conjugate deviation of the eyeballs to the opposite side. According to them, the frontal area presents marked differences of reaction from the motor area in the Rolandic region, and it seems necessary to put it in a separate physiologic category."

References dealing with eye movements in the cortex and particularly in the frontal are extremely important in works dealing with the autonomic. In the preceding pages we kept reiterating the fact that pupillary reactions are localized in many places in the hypothalamus. That the above as well as eye movements also are localized in the diencephalon and centers below may be seen from the following series of quotations.

"Long before the investigations mentioned, Schäfer (1888, 1889) demonstrated oculogyric movements by electrical stimulation of the occipital lobes. Barany, and Cecile and Oskar Vogt (1923) found differences in faradization of the foot of the second frontal convolution from that of the calcarine area. In the former the movements of the eyes occurred sooner and lasted much longer than in the latter. Dejerine and Roussy (1905) reported conjugate deviation of the eyes in a case of congenital blindness in which there was an occipital lesion.

"Heitz and Bender (1901) stand alone in their claim to have seen a case of softening of the posterior part of the temporal lobe that caused lateral conjugate deviation of the head and eyes."

Those who are not trained in the neurology of epilepsy might be struck by a seeming lack of relationship between conjugate deviation and gastrointestinal

phenomena. Let it be remembered here that conjugate deviation forms part of almost every epileptic attack and that its autonomic accompaniments cannot be unrelated to the corticodiencephalic pathways. The scope of such pathways and therefore the extent of the corticodiencephalic connections can be envisaged by the quotations which we are presenting.

The following quotations are taken from Davison and Goodhart (1931):

"*Centrum ovale*:—As the oculogyric and cephalogyric fibres are close together, lesions of this area will frequently involve both types of fibres with resulting conjugate deviation of the head and eyes. In exceptional cases the head may turn one way except by a lesion destroying the oculogyric fibres and compressing or causing irritation of the cephalogyric fibres or vice versa. Such syndromes were observed by Prevost (1869), Grasset (1904), and Roussy and Gauckler (1904).

"*Cerebellum*:—Lesions of the cerebellum may induce lateral conjugate deviation. These have been demonstrated by André-Thomas (1897) experimentally, but the deviation in these cases is evanescent, lasting at most a few days."

H. A. Riley (1919) in the report of a case of oculogyric spasm to the right, somewhat similar to ours, with the exception of definite and permanent sensory disturbances of the right side of the body, placed the lesion clinically, "in the mesial fillet in its internal portion, together with the pes lemniscus superficialis contained within the fillet and the emergent fibres of the oculomotor nerve of the left side as it passes through this part of the mesial fillet". Let the modern electroencephalographer who records a three per second frequency in a petit mal case with oculogyric phenomena note the deep seated relationship between the bioelectric, the clinical and the anatomic by referring to our quotations above. Let him realize furthermore that these are directly connected with the autonomic and can in no way be separate from the cortical representations that constitute the cortical regulators of gastrointestinal function.

Before our quotation of the summary of Davison and Goodhart we will digress with a few remarks. It is surprising that Davison and Goodhart who have dealt a great deal with the extrapyramidal tract did not include oculogyric crisis seen in cases of mesencephalic encephalitis. We are also surprised that they failed to include certain convulsive eye movements such as Tilney and Riley (1923) described in association with a syndrome such as Foville. In such a syndrome the eyes look on the paralyzed side which is contralateral to the lesion in the mesencephalon. In our experience with cases of epilepsy we have never come across such a form of epilepsy. We believe however that not only is the mesencephalon involved in various types of abnormalities in eye movements but that the diencephalon may also be responsible for it. We are surprised that the above authors did not include additional structures above the mesencephalon and others below the centrum ovale.

In the preceding data we have shown that pupillary reactions are obtained in association with eye and head movements on stimulation of almost all lobes of the cerebrum. In some instances the brain stem stimulation produced similar

reactions. The route of these and similar reactions is through the base of the cerebrum and that of the autonomic reactions mostly through the diencephalic portion of the hemisphere. From the previous study we have realized that there are essentially two schools of thought with regard to the neurogenic control of the gastrointestinal and urinary system. The first consists of the great modern workers on the mammillothalamic tract. Among these are Greving, Malone, Morgan, Muskens, the great number of authors analyzed by the presentation of Donal Sheehan, and the authorities presented in the paper by Hare. This includes many authorities who started work as far back as 1860. The second school favors the pyramidal and attaches the autonomic functions to this system mostly on a clinical basis. These authorities concentrate upon the area gigantopyramidalis and annex the parietal, temporal, and occipital lobes to this pathway. This school consists of a great number of investigators mentioned by Watts and Fulton including among them Bechterev, Bochefontaine, and many others. It seems that the group of authorities mentioned by Davison and Goodhart automatically fall into the latter category. Our previous presentation of the scheme of the sympathetic system as offered by Rosett indicates that although he includes the hypothalamus he tends to favor the pyramidal pathway. In his presentation of his diagrams, he oversimplifies the autonomic in relation to the pyramidal. This tendency to oversimplify and make out of the entire central nervous system a neurotopographic bicellular system was probably intended for the purpose of offering to the bioelectric neurophysicist a system by which to explain on their basis, a mechanism involved not only in autonomic and somatic function but also that of the convulsion.

From the above data we realize therefore that a great deal of independent material taken from neuroanatomy can be correlated with an equally great amount of substance taken from clinical neurology. Both of the above can be therefore finally united so that the corticobulbar and the lobopontine tract be given their place together with the corticorubral, corticonigral and tectospinal and olivospinal in the realm of diagnostically important structures. From the following summary of Davison and Goodhart and the remark in quotation by Rosett we can see how both of these systems of the autonomic mentioned above are connected within the cerebral cortex. This should impress the reader with the upward destination of autonomic phenomena for which the diencephalon in general and mammillothalamic in particular are a thoroughfare. Later we will refer to their origin in the brain stem.

Summary from Davison and Goodhart:—"A case of oculogyric spasm without cephalogyric movements, subjective sensory disturbances on the right and a left homonymous complete quadrantic hemianopsia is presented. Pathologically there was a multiplicity of lesions of the cortex in the form of small areas of softening of the left postcentral, inferior, and superior parietal, angular, supramarginal and bilateral inferior occipital gyri, as well as a small lesion in the medial nucleus of the right thalamus. The main cortical center for movements of the head and eyes, the foot of the second frontal convolution, was free from any involvement. The lesions that explain the observation in this case were in the

left postcentral, superior and inferior parietal, angular and supramarginal gyri. As it is disputed whether this area is a center for oculogyric and cephalogyric movement, a possibility of involvement of the intercortical association pathways, the occipital frontal fasciculus, connecting the cortical visual area with the frontal centers for ocular muscles should be considered."

At the beginning of our anatomic presentation we referred to the bundle of a basket in giving a bird's-eye view of the anatomy of the corticodiencephalic system. All the data by Davison and Goodhart deals with only part of the top of the handle of the basket. Detailed reference to the rest of it will be given later.

A further remark on the above summary must be added to show that it was not necessary for Davison and Goodhart to stretch the connections between the area of the occipital as far forward as the frontal region. From their own references it would have sufficed if they connected parts nearer to the occipital region than the frontal namely, the temporal and other regions that have been shown to have oculocephalocervical movement functions associated with contralateral hemicorporal musculoskeletal movement. The areas which we have mentioned above were concentrated upon by Foerster and Penfield in relation to epileptic attacks. The above data further strengthens our assertion of multicortical hemicorporal tonus representations which are probably connected with the corticopontine and corticobulbar frontopontine and with the corticospinal and even corticorubral and strionigral etc., tracts which lead into the brain stem.

The issues involved in eye and head movements, as well as in other scattered functions, such as those involving autonomic pupillary and other activities in regard to the cerebral cortex, are brought out in the comment of Rosett upon the work of Davison and Goodhart: "The case presented cannot be depended upon for the localization of the oculogyric movements. The lesions were numerous and widespread. Goodhart's citation of opinions of the investigators who attempted to localize these movements is a little bewildering, since both stimulation as well as destruction of the frontal, parietal, occipital, and temporal lobe appear to have produced these movements. What little dependence can be placed on some of these results perhaps becomes evident because of the fact that a frontal fasciculus has been dragged in for the purpose of localizing movements. I am certain that this fasciculus does not exist. Adolph Meyer in his anatomic study of the visual pathway in 1907 (Transactions of the Association of American Physicians), came to the conclusion that there was no such fasciculus. In 1922 (Brain) I produced a series of microscopic sections prepared by a new method in such a way that an entire cerebral fibre system could, in a large part, be traced in a single slide, and in which minute bundles of fibres could be followed for several inches. These slides show definitely that what had been taken for a continuous bundle extending from the frontal to the occipital lobe really consists of two separate systems. One of these arrives from the frontal and prefrontal regions, and assuming for some distance a horizontal course, bends downward to enter the lateral nucleus of the thalamus; while behind, the fibres were merely those of the tapetum of the corpus callosum. The frontal occipital fasciculus, was discovered by Forel and Onufro-

witsch. The only evidence which they adduced for its existence was their observation of a gross specimen of the brain of an idiot with a defect of the corpus callosum. It owes its persistence to Dejerine, who, on the strength of the evidence just mentioned, committed the error of popularizing it in 100 pictures in his monumental work of the anatomy of the nervous system." "The case presented seems to me to be one of epilepsy. In this disease the movement of the eyeball to one side is not at all uncommon. Gowers has given a description of these movements which, for its beauty and accuracy, may be considered as a classic, and most of us have seen oculogyric movements in similar cases."

It is interesting to note that the thalamus forms part of the above system. This shows that the mammillothalamic and pyramidal systems, though somewhat

Fig. 24

distinct from each other in the lower portions of the cerebrum, are probably united in the cortex. The movements discussed above are intimately related to chewing, swallowing, etc., movements and most of such cranial movements are part of parasympathetic function. It is essential to note that the fibre tracts controlling them on their way down to the brain stem pass near or through the mammillary bodies which are near the gateway to almost all types of structures conducting sensory and motor impulses.

The above material makes us realize that the cephalocervical region is finally getting the prominence that it has deserved for a long time. We realize with the above that the human is a combination of the best taken from the avian and the most highly developed static characteristics of the mammalian so as to enable

him to function the way he does. When objectively observed one must realize that most of the conditioned as well as unconditioned activities during the walking stage consist of a great deal of eye, facial, and nuchal activities in all directions. This is true of the sitting as well as the walking state. In contradistinction to all other forms of animal life, the human is characterized by head turning and eye movement in all forms of communication, verbal or otherwise particularly associated with the sitting position. For such forms of conditioned and unconditioned activities it is therefore necessary that a wide range of representation within the cerebrum of cephalocervical activities be firmly established. Accompanying such activities there is, as we have seen, manifestation of autonomic activity via association fibres and the lateral thalamic nucleus.

It is therefore a surprise to find that with the march of development along the above lines there has been a similar development of the human in the cellular structure of the diencephalon that connects the mammillothalamic tract with the cortex and brain stem. This we see in the references by Kappers, Huber and Crosby. These authors state that the main mass of the nucleus mammilloinfundibularis or Greving's frontotuberal structure is situated at the ventrolateral periphery and grouped to extend up and around the fornix. The arrangement of cells appears to be somewhat more compact in man. However, in man not only is there a well developed lateral portion of nucleus which cephalically reaches the ventral surface of the diencephalon, but there is also a medial portion found internal to the fornix column. In their summary of the dorsal thalamus Kappers, Huber and Crosby state that the medial division, consisting of three nuclear groups is the most visceral dominating part of the dorsal thalamus. This structure derives its fibres from the floor of the diencephalon the cells of which are extensions from the cranial nerve nuclei of the tegmentum, particularly from taste and also olfactory and other structures. The above fibre tracts eventually, as do the cephalocervical fibres, end in the brain stem, and in this latter structure they are intimately connected as shown by the data of Kappers, Huber and Crosby. These authors state that from the tectum, motor fibres and their functional impulses are directed to the stem and cord and this is effected over the tectotegmental system, according to Winkler and Potter (1911), Tsai (1925a), and others. Kappers, Huber and Crosby also state that crossed and uncrossed tectoculomotor, and crossed and uncrossed lateral and medial tectobulbar and tectospinal tracts connect with the above system according to Edinger (1908), Ramon y Cajal (1900), Winkler and Potter (1911, 1914), Rasmussen (1931 and 1932), Tsai (1925), and Rioch (1929). That the red nucleus may also be connected through the mediation of the posterior commissure in the mammillothalamic tract and fortified in the brain stem is shown by the statement that crossed and uncrossed tectorubral tracts stretch to the diencephalon. The nuclear and commissural systems of the tegmentum are directly connected with the mammillary region. Pavlov (1900), Tsai (1925), and Rasmussen (1901), state that to the pontine gray pass the tectal fibre systems from the posterior mammillary passage. Tectonigral and nigrotectal paths have been described by Tsai (1925), Kodama (1929), and Rioch

(1929). Later we shall add references of the literature dealing with the trigeminal to this system. In doing that we will have a complete view of the cranial nerve system and its internuncials. From the above we can see how well fortified and markedly interconnected are various fibre tracts that descend from the cerebrum including the mammillothalamic system, as well as the cranial nerves responsible for eye and head movements which extend from the cortex to the brain stem. Kappers, Huber and Crosby state that the means of cortical conditioning of the tectal reflexes are provided by the corticotectal fascicle which swing down from the occipital region of the cortex, and through the dorsal thalamus and enter the tectum to the striatum and adjoining regions. From the seemingly digressive material in the preceding pages the reader will note that the work started by Karplus and Kreidl on the autonomic representation in the diencephalon has future promise in the great expanses of the telencephalic portions of the cerebrum. This is evidently likewise true for the work of Beattie on the gastrointestinal representation in the diencephalon, and the upward extensions into association systems (Rosett).

Above we have presented the necessary references to show that the lower portion of the mammillothalamic tract has been thoroughly investigated; that the experimental as well as the clinical material dealing with gastrointestinal and urinary function have been placed on a good neurogenic anatomical foundation and the above structure has been related to the pyramidal system and brain stem and the upward extensions of this structure terminate in the upper portion namely the thalamic portion of the mammillothalamic tract.

In the previous anatomical discussion of the mammillothalamic or the corticothalamomammillary tract we have invariably attempted to illustrate and give various references to the literature to prove that this tract is intimately connected with the anatomical polyhedron situated at the base of the cerebrum which is essentially connected with vegetative or autonomic function. We also showed the base of the diencephalon to be a continuation of cranial nerve structures of the tegmentum of the brain stem. We digressed on a discussion of eye, face and head movements. In this digression we placed on a firm basis masticatory, eye, and other movements and showed that these are essentially frontal and thalamic. There are fibres from the frontal areas probably connected in some way with the medial and lateral corticobulbar tracts which are situated in the foremost portion of the internal capsule. We were primarily interested in such autonomic functions because this is largely a work dealing with the neurogenic control of the gastrointestinal system. Our main effort has therefore been shown to be directed along the lines of vegetative neuroanatomy with gastrointestinal and related functions such as chewing and swallowing. That the vegetative nervous system, as manifested by contractions of the gastrointestinal musculature, may be related to long and short conduction phenomena and therefore to tonic and clonic phenomena and involve problems in tonus is another matter. Here and there we touched upon the diencephalon and other basal structures as centers for tonus. We gave as references the work of Sherrington, Rademaker, and others. We wish to confess that although

this work deals with the subject of neurogenic gastroenterology in epilepsy we nevertheless intend to confine most of our attention to the former rather than the problem of epilepsy. It is however, nevertheless befitting that since the problem of tonus involves both the gastrointestinal tract as well as the musculoskeletal system in the course of a convulsion, that we devote some little of our time to those centers of the brain that control this phenomenon, and to a little of the neurophysiology that concerns the same. This deviation from our discussion of the anterior nucleus of the thalamus and the upper portion of the mammillothalamic tract will serve us in good stead, since in our presentation of the literature on the anterior nucleus of the thalamus, there will be many references by anatomists and neurologists to ordinary tone as well as affective (mimicosomatic) tone as being localized in the diencephalon and in some portions of the frontal cerebral cortex.

Muskens (1928), besides doing a great deal of work on eye movement centers, posterior commissure and other areas, spent most of his life on the problem of the tonic and clonic reactions, convulsive fit and its physiology. Although he has dealt largely with epilepsy as a clonic phenomenon, in order to establish his theory of myoclonic shock, he has nevertheless given us an excellent view on tonus in relation to the convulsive syndrome. Although he regards almost all epileptic phenomena to be related to myoclonic reflexes that are present in normal children, his views of tonus should be acceptable because they have a good implication of bioelectric conduction rate and transmission frequencies and as such might apply to smooth muscle tonic phenomena.

Muskens is evidently right with regard to the physiologic relationship between the tonic and clonic phase of the convulsive fit as presented in the subsequent quotations. His concept of the localization of the fit in the extrapyramidal system may however not be acceptable to many authorities, particularly to those who have done great experimental work with Jacksonian epilepsy, which is essentially a cortical phenomenon and the pyramidal tract seems to be more elaborately connected with this type of epilepsy rather than the striatum. The following quotation is however of interest since it shows some relationship between muscle contraction on the basis of tonic phenomena and action currents: "Ordinary observations of the initial stages of a fit show the body stiffening in a tonic or cramp condition, but a graphic record of the phase did not show a corresponding tracing. On the contrary, all the tracings recorded by each of the four different methods showed the same evidence that if the condition were recorded with sufficient precautions, separate convulsions are individually discernible. Only at the end of the fit, when the single convulsions are more isolated, the clonic character becomes more pronounced, because the locomotor effect of the muscular contraction was allowed more space. This is why I have come to the conclusion that the whole doctrine of tonic and clonic convulsions which postulates fundamental difference between the tonic and clonic convulsions requires revision. This is more particularly the case, because some physiologists and clinicians tend to regard the tonic and clonic convulsions as functions of different structures in the central nervous

system. Those who are inclined to question the proposition that essentially there is no difference between tonic and clonic convulsions are referred to the electromyographical studies of Cobb. In this investigation, Cobb shows that the concomitant electrical changes are absolutely the same, the difference merely being that the 70 to 90 action currents per second occur in clonic convulsions in groups and showers, while in tonic convulsions they are continuous."

Tonus is probably an efferent phenomenon and involves intestinal tone as well as movement of eye, head and neck as seen in every fit. When Kappers, Huber and Crosby stated that the base of the diencephalon is largely an efferent structure they were probably right. They were cautious however when they established an anatomical relationship between the floor of the diencephalon and the extrapyramidal system. They merely assigned automatic associated move-

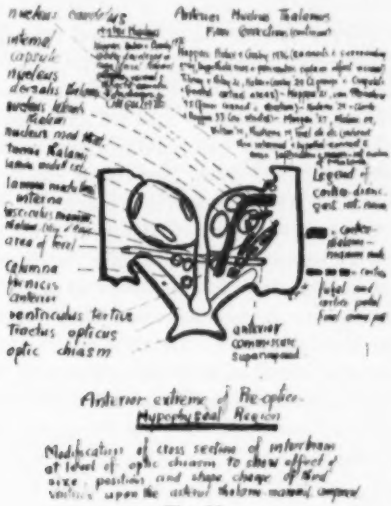

Fig. 25

ments to this anatomical combination and omitted at that particular time, conjugate and other head movements because only few authorities (Muskens) connect them with the striatum.

The problems brought out in the above quotation are all-inclusive ones. They cover not only the field of epilepsy, tetany, etc. but also the problem of permanent hypertonicity as is seen in transsection of the spinal cord, in decerebrate rigidity, and other conditions that are observable in almost every type of disease of the brain and spinal cord from multiple sclerosis to epidemic encephalitis. In looking around for anatomical pathways to explain the tonic gastrointestinal reactions which they observed in their experiments, Watts and Fulton finally chose the extrapyramidal pathways. We can see that they were right as far as musculoskeletal tonus is concerned since conditions such as dystonia musculorum deformans are produced by lesions in the striatum. This is, however, not true of gastrointestinal motor and

tonic phenomena since they have been shown to be controlled by the diencephalic centers which stretch into the tegmentum of the midbrain taking in commissural and nuclear bodies other than the extrapyramidal, except in one or two instances.

Although Muskens was definite in his opinion that essentially the tonic convulsion was composed of a number of clonic ones, there seems to be nothing at present to indicate that both of these had the origin of their impulses in the same anatomic location. If Muskens was of the opinion that the corpus striatum was responsible for the origin of both the myoclonic as well as the tonic convulsions, he will find a great deal of disagreement among experimentalists on the problem of epilepsy. The number of such workers is legion as will be shown in our attempt to give the physiology of the fit subsequent to our neuroanatomical presentation of the literature. We will then discuss the old ideas of centers of fits which have been heretofore located largely in the hypothalamus, brain stem and in the cerebral cortex. Many workers have localized the convulsion in the region of the third ventricle wall and in the region of the greatest neurogenic control centers of gastrointestinal and urinary function. In these places, the last mentioned being the most recent ones, it was felt by most of the authorities with whom one of us has a number of years ago been particulary associated (Pike, Notkin, Coombs and Weingrow), that the tonic portion of the epileptic fit is localized more in the parts distant from the cortex and the deeper portions of the cerebrum nearest to the diencephalon as well as in the mesencephalon; while the clonic convulsions, they felt, were localized mostly within the cerebral cortex. It is however possible that Muskens felt that the phenomenon of tonus as expressed in the convulsions was a combination of myoclonic reactions independent of anatomical localization. If such be the case, then, the cerebral cortex which is responsible mostly for clonic phenomena has produced the problem of the function of the dissociation in the tonic convulsion and split the same into clonic ones in the same way as the cerebral cortex has a tendency to dissociate the sensations of pain, temperature, tactile, vibratory, and other sensory perceptive faculties as well as motion, muscle strength, tendon reflexes, cranial nerve functions, and the trophic function of the body. The last mentioned may be noticed in the scattered places particularly of the wasting of small muscles of the body, and the unilateral muscles of the extremities usually noticed contralateral to the lesion in the cerebral cortex in most of our epileptic patients. The sum total of our anatomic and physiologic data amounts to the fact that the convulsive phenomenon is essentially a pyramidal tract activity phenomenon associated with diencephalic tonus accompaniments. Only in some cases of epilepsy such as those associated with neurosomatic deterioration rigidity do we see extrapyramidal tonic symptoms. This is probably due to degeneration of the thalamostriatal fibres. Muskens does not take our stand but the greater part of the literature points in our direction.

The problem of convulsions is of interest not only to the pediatrician as may be seen from the eventual quotation, but also to the gastroenterologist in particular and the internist in general because the fit, no matter whether it is due to brain tumor or uremia, or some other condition, is always associated with vomiting and

defecation even without definite preparoxysmal evidence of neurogenic central activity controlling the gastrointestinal tract. Although all the anatomic references point to the anterior nucleus of the thalamus which is part of its medial dorsal division as a center for visceral reactions, these have not been classified on an afferent or efferent plane. It is therefore not unlikely that motor and tonic gastrointestinal reactions are neurogenically controlled by the corticothalamomammillary system passing through this structure. Whether convulsive or nonconvulsive tonic conduction phenomena from the frontal areas also pass through it is uncertain. In the following quotation from Muskens we are interested in the problem of the epileptologist only insofar as tonus is a problem not only of epilepsy but also of tetany, and also that in the latter condition the optic thalamus, being a cellular structure, in order to chemically modify impulses must have elaborate fibre connections, with tuberal controlled endocrine structures.

"The fact remains that at the present day the different forms of infantile convulsions have not been properly classified, neither is there a proper appreciation of the connection which may exist between different convulsive symptoms seen by the pediatrist and the adult with fits or allied phenomena seen later by a neurologist. When a case of epilepsy in an adult comes under the care of a neurologist, it is often impossible to get a satisfactory early history of the case. Even where the patient has had infantile convulsions, and has been attended by a pediatrist, he has almost certainly been lost sight of by the pediatrist during the lapse of years. The parents or near relatives can rarely give a correct history, for years have dimmed the memory of observations, which probably were very incomplete and inaccurate. Further, it must be rememberd that even amongst the profession there is not a clear classification of the different forms of infantile convulsions. It is obvious, therefore, that amongst the laity the confusion is worse, and all sorts of conditions are referred to under the title of 'infantile convulsions'."

As in neurogenic gastroenterologic control centers and in neurogenic trophic centers not only fundamental clinical methods of attack have escaped the literature but basic principles are at times lacking in the field of convulsions. With all the modern advances in electroshock of the experimental and therapeutic type it is conceded by the mass of these workers that there is a central excitatory state which is thown into action by the electrodes in the same way as a battery starts off a generator. After acquainting the reader with the different phenomena that come under the heading of convulsion, Muskens classified his material into four groups of which the following quotation falls into most of the second group.

"In very young children, under one year, who are very ill, particularly with hereditary syphilis, tonic cramp, or tonic convulsive movements, sometimes occur. This phenomenon is frequently seen just before death. Observations made by Soltmann are of interest for this type of convulsion. Soltmann states that at this stage of life the pyramidal tracts are not yet functioning as in the adult; it is probable, therefore, that these tonic convulsions are due to a change or disturbances in the corpus striatum and not to the pyramidal tracts.

"Another interesting observation was made by Soltmann. He found that sixteen stimulae per second will induce tetany in the newly born animal, whereas in the adult, fifty stimulae per second are required. There is, therefore, a greater tendency to tonic convulsions in early life. Further, the muscular contraction curve is slower in type than with the adult. These two observations suggest the possibility of there being some etiological connection between the convulsive movements described under class #1 and myoclonic convulsions occurring later in life. Certainly the convulsions of class #1 are much slower than real myoclonic convulsions."

It should be emphasized that Muskens who proposed the myoclonic shock theory did not stress a central excitatory state as the underlying source of these shocks that constitute a major convulsion. With regard to localizing such a source he even broke away from his contemporaries by denying that the cortex or hypothalamus should be regarded with suspicion in that respect but he did stress the striatum.

We do not care to be involved in any argumentative feature on neurophysiology even though such might have clinical implications. Therefore we hesitate to offer our opinion with regard to the striatum, the pyramidal tracts, or even the optic thalamus as the regions of origin of either tonic or clonic convulsions. We do know, however, that the optic thalamus is a center for modification of the transmission of sensory nerve impulses. The ventral thalamic structures have furthermore been assigned efferent properties. In all our writings we have had the occasion to observe the fleeting sensory changes seen in the epileptic upon a careful neurological examination as well as the certain forms of aurae in which sensory phenomena precede the attack. We will even mention (Weingrow, Pigott and Fitch) six modifications of the Tinel phenomenon as observed in miliary peripheral nerve injury and spinal injury, and compare the above travelling phenomena with the Tinel sign. The convulsive state is therefore, as Muskens implied, a reflex-like reaction which may have a central tonus source. This source of tonus is probably in the same location for gastrointestinal musculature as it is for the striped muscles. The diencephalon is regarded by most modern workers as the main center for this all embracing source of tonus. It is therefore not unlikely that the simple rhythm of smooth muscle action seen in gastrointestinal and cardiovascular reflex activities has a central source in the diencephalon. With the above we will terminate the subject of tonus and proceed with the anatomy of the thalamus, that is the anterior nucleus of the medial division of the dorsal part of it.

Although Rosett made a brilliant discovery when he found that hyperpnea produced increase in tonus and convulsive phenomena, he never attempted to localize the origin of tonus in the anterior or other nuclei of the thalamus. If he ever did mention the thalamus in relation to tonus, it is certain that he never repeatedly referred to the same. The above was not done in spite of the fact that he knew that hypotonia is often found with certain syndromes of the optic thalamus. Although some types of syndromes have been associated with the optic thalamus, and it has often been blamed for a great number of functions which do

not seem to reside within it, the anterior nucleus of that structure has been, with the exception of gastrointestinal and urinary functions, relatively free from the assignment of some syndromes. The nucleus anterodorsalis of the thalamus (Kappers, Huber and Crosby) has been frequently designated as nuclei dorsalis disseminata by Marburg (1904), Sachs (1909a), and Ingvar (1923). This structure is located near the surface of the diencephalon. The principal anterior nucleus is termed the nucleus dorsalis magnus by Sachs (1909), and Marburg (1904). Von Monakow (1905), gives the same name for the human as for carnivore. Malone (1910), includes all the above under his nucleus reunions. Besides the nucleus dorsalis magnus it seems that the other two anterior nuclei are represented by a pars dorsalis and a nucleus commissuris thalami. The classification of the various subnuclear components of the anterior nucleus of the thalamus seems to involve disagreements. Foix and Nicolesco (1925) recognized in many only as a single nucleus anterior which they called the hauptkern or chief nucleus of Friedmann. Even in highly authoritative works on comparative neuroanatomy such as Kappers, Huber and Crosby we find that the citation of disagreements and the variety of names presented with regards to this nucleus or its parts leaves the reader in a state of confusion. This confusion is made worse when the question is brought up as to which parts of this structure are absent in the human. It might be best to designate the parts of the dorsal nucleus by their function viz. the medial nucleus as the olfactovisceral and the lateral as the somesthetic division of the pars dorsalis.

It has been shown by Kappers, Huber and Crosby, that Friedmann claimed that the cellular components of the anterior nucleus consist largely of multipolar cells that are polygonal in outline and Malone, in working on the diencephalon followed cellular character rather than nuclear configuration as done by other authorities. It seems that in following our presentation of the literature we shall stress not only the fibre connections of the anterior nucleus but also certain cellular characteristics. It is in this way that we can hope to clear up the missing anatomical parts necessary to connect the experimental neurophysiologic work on the gastrointestinal system by such investigators as Beattie, Sheehan, Keller and D'Amour who dealt with the diencephalon, with the extensive investigations of Watts and Fulton and others who dealt with the same subject from a cortical control approach. In our presentation of the neuroanatomy of the hypothalamus and mammillary region, we essentially followed the same course.

Kappers, Huber and Crosby, in discussing the nuclear pattern of the anterior nucleus of the thalamus presented an extensive bibliography. That cellular configuration is very important to the neuropathologist and to the neurophysiologist, has been shown by many bioelectric neurophysicists who proved the cells within the ganglion, particularly those within the autonomic nervous system, modify impulses which are transmitted to them and are present in the phenomena concerned with synaptic modification of bioelectric impulses. In our dealing with the mammillothalamic tract, we have found that the anatomists to whom we referred were rather wary of the last mentioned subjects. Cellular configuration, although

extremely important has, at this stage of the rather limited clinical application of thalamic function, little to offer us. We will therefore, omit extensive detailed bibliographic or other comments on this subject and proceed to attempt a detailed presentation of the fibre connection of the anterior nucleus of the thalamus which forms a way-station for our proposed neuroanatomic elaboration of the cortico-thalamomammillo-mesencephalopontobulbospinal autonomic tract.

Kappers, Huber and Crosby state that the nucleus anterior dorsalis of the thalamus is connected in man according to Dejerine (1901) and Von Monakow (1905), to the medial part of F-1 and gyrus fornicatus (cingulate) of Forel (1907). Internuclear fibres connect it with adjoining nuclear groups (Gurdjian), with the anterior group and (d'Hollander), with the lateral nucleus. Ramon y Cajal carried mammillothalamic fibres to this group. Recent experimental work indicates it is present in the dog (Glorieux, 1929 and Le Gros Clark, 1932a). Further evidence that the nucleus thalamus anterior (ventral group) receives mammillothalamic connections in man (Von Kolliker 1896 and Dejerine 1901), and that it has connections with the telencephalon in man has been shown by Sachs (1909a), Dejerine (1901), Forel (1907), Foix and Nicolesco (1925). Fibres were also believed to be carried to the anterior nucleus of the thalamus from the internal capsule. Villaverde (1923) believed that destruction of motor cortex in the rabbit led to the degeneration of the cortical thalamic bundle to the anterior ventral subnucleus of the thalamus. Le Gros Clark (1932a), destroyed the cingulate cortex in the rat and obtained results comparable to those obtained by Villaverde. From the above we can see that it is not necessary for one to connect gastrointestinal neurogenic fibres from the cortex with the extrapyramidal system as Watts and Fulton have done. The above proves that there is a shorter route through the thalamus to the mammillary system which is proved experimentally to control gastrointestinal functions. Le Gros Clark suggested that the results of Villaverde were due to the depth of the lesion destroying the path of the cingulate gyrus. Noting the above we can readily see how the anterior nucleus of the thalamus, connecting with the cerebral cortex associates gastrointestinal, urinary, and other autonomic functions with the phenomenon of tonus and motion thus combining autonomic with pyramidal control. This evidently forms a small portion of the combination of which the area gigantopyramidalis is capable. It must be remembered thus that this area contains large cells which number about 80,000 in man and that the processes of the cell extend down into the various levels of the spinal cord. When Rosett in his scheme of the combination of autonomic with pyramidal tracts tried to simplify the central nervous system into a topographical bicellular structure, he did not go so far afield. He might have stretched a point by connecting motor and sensory into one continuous working scheme. Whether such a connection is possible on a bioelectric basis remains to be seen. Muskens, however, did not attempt such a correlation. Although Watts and Fulton maintained that it was the premotor rather than the motor area that controlled gastrointestinal motor reactions, they did not completely exclude the latter or even the postcentral area. Muskens adhered mainly to the motor manifestations of the epileptic attack claiming that tonus is reflected as a continuous reaction in the

grand mal tonic epileptic attack which is a combination of myoclonic reflexes. He, on the other hand, was attracted more to the extrapyramidal system in which tonic reactions are more often seen. He stressed the medial longitudinal fasciculus and its extrapyramidal connections as having parasympathetic gastrointestinal functions by its connections with cranial nerve chains. If he had his way he would probably term the oculogyric reactions seen in encephalitis as a tonic reaction consisting of a combination of multiple myoclonic reaction. The tonus function as placed by many authorities in the diencephalon is therefore from the above seen to be extended also in cortical areas. Here one sees, therefore, tonus combined with parasympathetic cranial nerve action of head movement linked to sympathetic pupillary functions. The reader will see how our digressions to Davison and Goodhart have explained the autonomic patterns.

Fig. 26

The mammillothalamic tract probably contains autonomic fibres concerned with tonic reactions in the gastrointestinal and other smooth muscle systems. Whatever functions the anterior nucleus of the thalamus might have it should be stressed that such are visceral and related to those of the mammillary region. In rodents, mammillothalamic fibres were carried to the anteromedial group by Ramon y Cajal (1911), Le Gros Clark (1932a), d'Hollander (1913), Rioch (1931) and Gurdjian (1927). Small mammillothalamic connections for the anteromedial nucleus of the anterior nucleus of the thalamus in insectivores were described by Le Gros Clark (1929a). Kappers, Huber and Crosby, state that the anterior nucleus of the thalamus has commissural fibres and that internuclear fibres are also present and that Munzer and Wiener (1902) and d'Hollander (1913), have shown connections with the telencephalon in the rabbit. The evidence for such connections has not received general corroboration. From the above it

is concluded that by internuclear we mean the other nuclei of the thalamus, and hence an extensive connection with the other parts of the cerebrum by the mammillothalamic tract can be expected. There is no doubt that in all our anatomic discussions of the mammillary region as well as of the thalamus, the reader has noted mostly autonomic features of gastroenterology. The reviewer can therefore see that all we have been doing throughout our seeming involvement in technical phraseology was placing on a firm basis the route taken by impulses producing motor gastrointestinal responses. We are therefore elucidating the meaning of the experimental observations of Beattie, Sheehan, Cushing, Karplus and Kreidl, Keller and D'Amour, etc., etc.

Rioch (1931), stated that the nucleus anteromedialis receives fibres from the anterior thalamic radiations and the inferior thalamic peduncle in carnivore (conceivably such fibres may be either cortical or striatal) but Le Gros Clark (1932) found no evidence that the anteromedial nucleus is connected with the cortex in the rat. Further evidence that the mammillothalamic tract through the anterior nucleus of the thalamus is connected with various portions of the cerebral cortex may be found in the following. Kappers, Huber and Crosby, state that the anterior nucleus of the thalamus contains masses in its anterodorsal regions that have connections with the cingulate region of the telencephalon but less probably with the striatum in most mammals. These anatomists are therefore not in agreement with some of their contemporaries who assign extrapyramidal functions to the cingulate gyrus. It seems more likely that they favor the neurogenic gastrointestinal control by the cingulate system. The anteromedial group of cells in the anterior nucleus of the thalamus also has a telencephalic path with the gyrus cinguli (fornicatus rather than with the striatum). Expermental evidence suggests that all three groups receive mammillothalamic fibres but that the anterodorsal group receives less of this system than the other groups. The lateral part of this dorsal division is pierced by the intercortical system (Rosett).

Kappers, Huber and Crosby, state that the anterior nuclear group is related by short internuclear fibres with the surrounding gray and probably with the hypothalamus, through the periventricular system. From the above we see how the anterior nucleus of the thalamus connects not only with the structures previously mentioned but also with certain parts of the anatomical polygon or polyhedron which we described to the reader in detail in the presentation of a bird's-eye view of the cortical diencephalic neurogenic structure controlling gastrointestinal and urinary function. In the foregoing we mentioned the periventricular system of fibres in our anatomical polygon scheme. We are almost certain that an appreciable number of the writers on neural gastroenterology and on water metabolism control would ask why we haven't stressed the periventricular system at least fifty per cent as much as we have the mammillothalamic chain. These investigators probably feel that the periventricular system with its dorsal longitudinal fasciculus that end caudally in preganglionic efferents of the brain stem is just as important as an autonomic system. Our answer is that we agree with them and that we would add to the above the fibres of the preoptic component of the

striae terminalis. The anterior nucleus of the thalamus as the way station of the mammillothalamic tract is claimed by Kappers, Huber and Crosby to be a center for correlation for visceral, predominantly olfactory, impulses with somatic impulses and a region of relay of such impulses in correlation to higher centers.

In man it may form together with the medial nuclear group of the anterior nucleus of the thalamus, a part of the discharge pathway for feeling tone through intracortical connections of the cingulate and frontal cortical areas according to Tilney and Riley (1921), and Huber and Crosby (1929). It seems that there is no doubt that the anterior nucleus of the thalamus as a whole comprises the anterior, medial, ventral and dorsal subnuclear groups and has many connections with the above as may be seen from the previous references to the literature and the references to follow. The bone of contention lies not that such connections exist, but as to whether the independent subgroups are related in toto or by themselves to certain specific structures. These structures cover not only the lower centers and the other parts of the optic thalamus as well as the interventricular fibres but also the telencephalic basal ganglia such as striatum as well as certain specific cortical structures such as various parts of the frontal, prefrontal, premotor, motor cerebral cortex as well as particularly the cingulate gyrus (gyrus fornicatus).

Von Monakow (1895) believed that there is a connection between the anterior thalamic nucleus particularly the nucleus anterior ventralis and the striatum apparently regarding such fibres and striofugal. Ariens Kappers (1921), suggested that the anterior nucleus of the thalamus is connected with the striatum by the thalamostriate fibres. Sachs (1909) described connections between the anterior nucleus of the thalamus and striatum, but recently such connections have been denied by Kodama (1929), Le Gros Clark and Boggon (1933). Part of the above, plus an instance of striatal stimulation are the only material which would support Watts and Fulton in their claim that gastrointestinal control is carried from the premotor cortex through the extrapyramidal system. Even if such were the case this would take place for a short distance eventually reaching the thalamomammillary system. The above data is interesting because it makes the mammillothalamic tract, particularly the anterior nuclear portions which are directed towards the cortex, a less complicated one by connecting it with the striatum. It is the individual corticothalamomammillomesencephalic pathways which are concerned with gastrointestinal and urinary function. If it also has the function of tonus to the autonomic structures it is at least not complicated by the striatal fibres which are known to be carrying tonus of an extrapyramidal type to the musculoskeletal system. There is however, definite evidence that the tract described above connects by the medial and other nuclear groups of the thalamus with the hypothalamic region. This may be seen from the data of Kappers, Huber and Crosby who state that fibres from the ventral division of the ansa lenticularis pass into the diencephalon (Morgan 1927), through fibres to the mammilloinfundibular nucleus of Malone (1909). These fibres of the ansa lenticularis evidently enter the diencephalon in the region of the hypothalamus. That the hypothalamus is connected

with the thalamus itself has been repeatedly established. We stress every possible feature of extrapyramidal gastrointestinal control because we feel that once and for all the gastroenterologist and neurophysiologist must decide whether they will accept the diencephalic fibre systems for their studies or look elsewhere. By diencephalic we mean not only the mammillothalamic but also the striae terminalis system, the dorsal longitudinal fasciculus system and the forward extensions of these three at the base of the diencephalon constituting the Friedmann-Cajal loop. It, therefore, may be definitely concluded that the anterior nucleus of the thalamus with the collateral and internuclear short fibres is connected with the mammilloinfundibular system through the hypothalamus. That such a connection continues downward through other structures is shown in the statement that the lenticular fasciculus described above has fibres that go to the nucleus of the field of Forel (Morgan, 1927), to the zona incerta and capsule of the red nucleus of the same and opposite side, (Wilson, 1914). The downward connection of the fibres near the hypothalamus as well as the usual route of the mammillothalamic tract has been established previously by us, and its destination in the medial longitudinal fasciculus has been repeatedly emphasized in the literature. These fibres from the anterior nucleus of the thalamus carrying gastrointestinal control functions and running from the field of Forel probably join with the medial longitudinal fascicular chain rather than with that of the red nucleus. Those who favor gastrointestinal control by the red nucleus probably have in mind the vomiting seen in cases of Ménière's disease where the dentorubral and vestibular systems are affected and possibly the gastric symptoms of tabes dorsalis.

(*To be continued*)

CHAPTER ACTIVITIES

Cuban Chapter

The Cuban Chapter of the National Gastroenterological Association has held elections for officers for the year 1950-51. Those elected are President, Dr. Pedro A. Barillas; Vice-President, Dr. Fernando Milanes; Secretary, Dr. Orlando de los Heros; Treasurer, Dr. Laureano Falla; Members of the Executive Board, Dr. Hector Madariaga, Dr. Jose Luis Lluch, Dr. Amado Grabiel.

New Jersey Chapter

A meeting of the New Jersey Chapter of the National Gastroenterological Association was held in Newark on 20 March 1950.

The speakers of the evening were Dr. J. Gerendasy who spoke on Rectal Reflex and Dr. A. I. Friedman who spoke on Regional Ileitis.

The following resolutions were adopted at this meeting:

"WHEREAS: Dr. Hyman I. Goldstein of Camden, New Jersey, one of the charter members of the New Jersey Gastroenterological Society, possesses a profound knowledge of clinical medicine, gastroenterology and medical history and has made most valuable contributions to the medical literature in these fields and;

"WHEREAS: he has won and retained the admiration and respect of his colleagues who recognized in him a fine gentleman, a great scholar, and an astute clinician as well as a noted medical historian,

"BE IT RESOLVED: that the New Jersey Gastroenterological Society fittingly honor their most gifted member, Dr. Hyman I. Goldstein, by tendering him a testimonial dinner at Asbury Park, New Jersey on June 11, 1950."

New York Chapter

The clinical meeting of the New York Chapter of the National Gastroenterological Association will be held at the New York Academy of Medicine on Monday evening, 10 April 1950.

The program for the evening will consist of: "Diaphragmatic Hernia Through the Foramen Morgagni" by Dr. Leonard Shapiro; "The Role of Cystic Duct Stump Pathology in the Postcholecystectomy Syndrome" by Dr. Michael Weingarten; "Ulcer Surgery with Gastroileal Anastomosis" by Dr. Charles Windwer; "Experience with an Improved Gastroscope" by Dr. Harry Barowsky; "Localized Linitis Plastica Simulating a Benign Lesion" by Dr. Roy Upham; "Histamine in the Treatment of Peptic Ulcer" by Dr. Benjamin M. Bernstein; "Chronic Ulcerative Colitis with Congenital Polyposis of the Colon" by Dr. William Z. Fradkin; "Syphilis of the Rectum" by Dr. William Lieberman; "Lymphosarcoma of the Stomach" by Dr. N. W. Chaikin and "Discovery of the Cause and Cure of Gastrointestinal Ulcers" by Dr. Josef S. Smul.

Members of the medical profession are cordially invited to attend.

NEWS NOTES

Hotel Reservations for 1950 Convention

Post cards for convention hotel reservations were sent to each member of the National Gastroenterological Association along with the March 1950 issue of the Monthly Bulletin.

Those planning to attend the Convention on 9, 10, 11 October 1950 and/or the Course in Gastroenterology immediately following on 12, 13, 14 October 1950 are urged to fill out and return the card immediately in order that they may be assured of hotel accommodations.

Executive Board Meeting

A meeting of the Executive Board of the National Gastroenterological Association was held in New York City on Wednesday afternoon, 15 February 1950.

Routine administrative correspondence was presented and ordered properly disposed of.

The Association was advised of the death of Dr. Eugene L. Armstrong of Los Angeles, Calif. and the usual letter of condolence was to be sent by the Secretary.

Dr. Roy Upham, Secretary-General, reported that the Boston Chapter was holding a meeting that evening at the U. S. Marine Hospital in Boston, and a scientific session would follow the dinner being tendered to the members.

He also reported that the New Jersey Chapter had held a meeting on 16 January 1950 at the Jersey City Medical Center and that the next meeting would be held that evening.

The next meeting of the New York Chapter will be held at the New York Academy of Medicine on 13 March 1950.

Upon recommendation of the Argentina, Boston, New Jersey and New York Chapters, the applications of the following were ratified as indicated: Dr. Hector Enrique Guaita, Buenos Aires, Argentina, S.A., Member; Dr. Raymond A. Dillon, Winchester, Mass., Member; Dr. Robert Horowitz, Jersey City, N. J., Member; Dr. Morris Klatzko, Brooklyn, N. Y., Member; Dr. Bruno Oscar Charles Pribram, New York, N. Y., Associate Fellow.

Dr. Joseph McKinley Rossen of Cleveland, Ohio was elected to membership at large in the National Gastroenterological Association.

Dr. Samuel Weiss, Editor of The Review of Gastroenterology, presented a monthly financial statement, which statement was accepted and ordered filed.

The Program Committee reported that the tentative program for the Course and Convention was ready and submitted it to the Board for approval, which approval was received.

Dr. Elihu Katz, Treasurer, reported that several members of the Association who had been advised that they were in arrears for two years had not paid their

membership dues and recommended that they be dropped from membership in the organization. Upon motion, duly made, seconded and carried, it was so ordered.

New Proctological Journal

The American Journal of Proctology, official publication of the International Academy of Proctology, made its initial appearance in March 1950.

The journal, a quarterly, under the editorship of Dr. Alfred J. Cantor of Flushing, N. Y., will be devoted entirely to proctology and allied subjects.

The material to be published will be directed not only to the specialist but to the general practitioner who is faced with proctologic problems in his daily practice.

In addition to original authoritative articles, the journal will contain abstracts of all current literature dealing with proctology and allied subjects as well as reviews of books on the subject.

The first issue contains the following articles: "Duodenocolic Fistula" by Dr. Earl J. Halligan, Dr. Louis L. Perkel and Dr. J. Kenneth Catlaw; "Malignant Rectal Polyps, Fulguration Versus Resection as Treatment of Choice" by Dr. Caesar Portes; "Combined Posterior Sphincterotomy and Pectenotomy" by Dr. Donald C. Collins; "Ulcerative Colitis" by Dr. H. M. Eberhard and Dr. Rowland Ricketts; "Sigmoidoscopy" by Dr. Horace Wendell Soper.

The subscription to the journal is $2.50 for one year, $4.50 for two years. Subscriptions may be sent to *The American Journal of Proctology*, 1819 Broadway, New York 23, N. Y.

Oral Examinations in the Subspecialty of Gastroenterology

The American Board of Internal Medicine announces oral examinations in the subspecialty of Gastroenterology to be held as follows:

14, 15, April 1950 at Boston, Mass.
23, 24 June 1950 at San Francisco, Calif.

These examinations are for candidates who have been certified in Internal Medicine and who have made application and passed the requirements for examination in Gastroenterology.

Further information can be obtained by writing to Dr. William A. Werrell, Assistant Secretary-Treasurer, 1 West Main Street, Madison 3, Wisconsin.

ABSTRACTS

GASTROINTESTINAL TRACT

HIDDEN GASTROINTESTINAL LESIONS. R. P. Reynolds and M. O. Cantor, Gastroenterology. 13:280-284, (Oct.), 1949.

The authors report four patients in whom gastric lesions could not be demonstrated preoperatively and one patient in whom even at operation the true gastroduodenal lesion was not found.

A negative roentgen report, if it does not agree with the clinical findings, should not be acceptable. Posterior wall ulcerations may be missed, even at operation, if the stomach is not opened.

In some of these cases which puzzle the radiologist, surgeon, and internist exploratory operation may be the only method of arriving at an accurate diagnosis. HYMAN I. GOLDSTEIN

ESOPHAGUS

ESOPHAGEAL ATRESIA WITH TRACHEOESOPHAGEAL FISTULA. T. H. Ingalis and R. A. Prindle. New England J. Med. 240:987-995, (June 23), 1949.

A report of 107 cases of esophageal atresia of which 102 had an associated tracheoesophageal fistula is given. There were anomalies of the cardiovascular, gastrointestinal, genitourinary, respiratory and skeletal systems in many of these cases. The causative agents of the atresia must be primarily genetic or else acquired in utero. None of the cases revealed this defect in successive generations nor were there any recurrences in the same generation of a family.

There is a significant association of congenital esophageal atresia with hydramnios. Some of the mothers experienced antepartum hemorrhage. Others developed acute infections or metabolic disturbances. These complications occurred between the first and third months of pregnancy. The authors point out that one must give thought to the probability that these congenital malformations may be acquired and are not necessarily departures from normal. A. X. ROSSIEN

STOMACH

REGIONAL ILEITIS. E. Calder. Glasgow M. J. 30:65-81, (Mar.), 1949.

A description of this disease from the pathologic, roentgenologic and clinical aspects is thoroughly presented. The literature is quoted and goes back to 1903 when Koch first described this disease. The various synonyms and the authors mentioned who have described this disease were Koch (1903), Dalziel (1913), Moschowitz and Wilensky (1923), Coffen (1925) and Mock (1913), all of whom ante-date the description given in 1932 by Crohn, Ginzburg and Oppenheimer. Since then many other observers have studied what is frequently referred to as Crohn's disease and have added considerable information relative to it.

The course and prognosis of regional ileitis is apparently variable in spite of the voluminous accumulated literature.

X-ray data in the early stage is unreliable since it is not definitive during the acute or subacute stages. There is a tendency to attribute nonspecific inflammatory conditions limited to the ileum as Crohn's disease. Unless a link can be established between the early nonspecific process and the advanced stages in the same patient, it is unlikely that the condition is Crohn's disease which should progress to the chronic phase.

The diagnostic significance of the roundish elevations on the mucous membrane of the terminal ileum as being indicative of early Crohn's disease is disputed. Further, Calder expresses doubt that spontaneous recovery from acute or subacute nonspecific regional ileitis is a distinct pattern for Crohn's disease. The author describes a honeycomb pattern of the x-ray appearance of the ileal mucosa and states that a close correlation exists between that pattern and the simple type of recoverable regional ileitis, with the implication that it is a separate entity from Crohn's disease.
A. X. ROSSIEN

CICATRIZING ENTERITIS, COLITIS AND GASTRITIS. J. R. Ross. Gastroenterology. 13:344-350, (Oct.), 1949.

Since the article (1932) by Crohn, Ginzburg, and Oppenheimer, a new cycle of interest was initiated in cicatrizing enteritis (ileitis). The author reports a case of "chronic ulcerative colitis (inactive phase)" on 4th hospital admission. On 5th admission (February 1949) the patient, a young single white woman, had a partial gastrectomy and gastroduodenostomy. At this time there was evidence of phlegmonous gastritis with ulceration, probably extension of the original cicatrizing enteritis (August 1946). On the first admission (August 1946) this young woman was found to have been suffering since January 1944, with cramp-like abdominal pains, intermittently, and associated with diarrhea. In April 1945 an appendectomy was performed and a diagnosis made of regional ileitis! The operation did not relieve the patient. In April-June 1945, rectal abscesses developed.

In August 1946, laparotomy was done and resection of the terminal ileum and right colon with primary anastomosis was accomplished. In November, 1947, "ulcerative colitis" was diagnosed—and, the patient was again submitted to operation and divided ileostomy; the diagnosis made was "recurrent ileitis with chronic ulcerative colitis". In December 1947, because of a nonfunctioning ileostomy and severe abdominal pain—she was again submitted to operation. A new revision and implantation of ileostomy was done. At the fourth hospital admission (August 1948) a last stage colectomy was performed—(a Miles abdominoperineal resection). The lesion in the stomach was identical with the cicatrizing ileitis. The colon, also, was characteristically involved!

HYMAN I. GOLDSTEIN

DIAGNOSTIC AND THERAPEUTIC CONSIDERATIONS IN MANAGEMENT OF THE ACUTE ABDOMEN. O. H. Wangensteen. Northwest Med. 48:315-318, (May), 1949.

The importance of history, physical examination and laboratory procedures including x-ray studies is re-emphasized as an aid in the management of the acute surgical abdomen. As the author states, there is nothing new in this article but the importance of early surgical intervention is so well brought out that this article bears endorsement of careful re-study and cognizance taken that surgical procrastination is the biggest factor in fatalities occurring in these patients. A. X. ROSSIEN

NEWER ASPECTS OF PEPTIC ULCER THERAPY. A. H. Aaron, William F. Lipp and E. Milch. J.A.M.A. 139:514-518, (Feb. 19), 1949.

The authors state that innumerable articles covering every phase of the diagnosis and treatment of peptic ulcer have appeared during the past year. Of course, all too many articles purporting to add many new methods of treatment, have been appearing for the past ten or fifteen years! Most of our so-called "modern and new treatments" for peptic ulcer—are nearly all "rediscoveries" or repetitions of old forms of treatment, that have been used for decades, and even for many centuries! We have, of course, made great advances, and considerable improvement in the accuracy of our diagnosis—but, as to treatment of peptic ulcer, we have not made very great progress.

The authors feel that it is almost universally agreed that peptic ulcer in the stomach and duodenum is directly related to the presence of hydrochloric acid and pepsin in appreciable amounts in the gastric contents. The production of anacidity by antacid therapy will control or prevent peptic ulcer. The authors speak erroneously of "medical vagotomy"—by the use of belladonna extract in effective dosage—i.e. in "tolerance doses", shown by dryness of the mouth and blurring of vision. In the authors' experience no preparation except one of the belladonna group accomplishes this result.

The barbiturates are only mentioned as central acting agents—as an additional aid.

All peptic ulcers in 85 per cent of cases will respond to acid-pepsin control—i.e. medical treatment plus central and vagal therapy based on education, sedation, and the use of the belladonna series in "tolerance doses".

Sixty per cent of ulcers will recur in persons so treated! It would, therefore, appear from this statement that with sixty per cent of failures—we have not advanced far with "medical vagotomy"! The control of these recurrences is our problem. The authors state that one of the foremost advances in treatment of peptic ulcer in recent years is the control of these recurrent ulcers.

The authors refer to the use of enterogastrone by Ivy, et al (1944, 1945, 1946) of Chicago—and their administration of an extract of duodenal mucosa rich in enterogastrone, which was remarkably effective in preventing the formation of postoperative jejunal ulcer in dogs (Mann-Williamson).

The authors have injected daily doses of enterogastrone in ten male patients—for periods of two to eleven months. However, the results were only fairly encouraging. Four of the six duodenal ulcers failed to respond. Two showed improvement of symptoms with healing of the ulcer. Of course, improvement of symptoms and healing of the ulcer have been noted with and without any and every form of therapy.

The authors refer to various operative procedures, including high gastric resection. 153 high gastric resections were performed at the Buffalo General Hospital 1940-1946. Eighty per cent of these patients had no free acid, when rechecked during 1947.

They feel that the patient with gastric ulcer who does not definitely improve with healing of the ulcer in four weeks should be operated upon. They do not temporize with gastric ulcer. Massive hemorrhage is treated with large blood transfusions—as much as 5,000 cc. (5 litres) may be administered in six hours—and prompt operation i.e. in cases of patients suffering from massive hemorrhage: continuing bleeding with classic picture of collapse. HYMAN I. GOLDSTEIN

BOOK REVIEWS

STUDIES IN PSYCHOSOMATIC MEDICINE. Franz Alexander, M.D., and Thomas Morton French, M.D. 568 pages. The Ronald Press Company, New York, N. Y., 1948. Price $7.50.

This comprehensive volume on Psychosomatic Medicine is divided into eight sections dealing with the various parts of the human anatomy. An ample bibliography follows each section.

Psychological factors in gastrointestinal disturbances written by Franz Alexander, one of the coeditors, deals with the influence of psychic factors on gastrointestinal disturbances. On page 107, the author states that "the patients' conscious psychological processes play a subordinate role in the causation of somatic symptoms, since such conscious emotions and tendencies can be freely expressed and relieved through the voluntary system". He further states "repressed tendencies, however, lead to chronic innervations causing chronic dysfunction of the internal organs".

Another example of conflict and emotion is mentioned on page 114, where the husband found that he had married a woman who was a superior person. He developed pain a few hours after meals and finally a gastric hemorrhage occurred.

This one example shows that it is the thwarting of receptive cravings, and not a certain personality type, that is of primary importance.

The relationship between gastric neurosis and gastric and duodenal ulcer is stressed.

Interesting theories are brought to our attention regarding colitis, especially the mucous and the spastic type. On the other hand constipation is also considered as a possible psychosomatic problem and several illustrative cases are cited.

Bronchial asthma, cardiovascular manifestations, hypertension, pruritus ani, urticaria and other dermatological conditions are discussed.

The book is interesting and helps to solve many of the questionable syndromes which do not yield to the physician's ministration. It is recommended and will be found helpful when borderline cases require careful study and analysis.

HOW TO BECOME A DOCTOR. George R. Moon, A.B., M.A., Examiner and Recorder, University of Illinois College of Medicine, Dentistry and Pharmacy. 131 pages. The Blakiston Company, Philadelphia, Pa. Price $2.00.

Prospective students of medicine, dentistry, pharmacy, optometry, etc. should read this informative book. It will be of material aid in seeking entrance to preprofessional and professional schools.

PSYCHODYNAMICS AND THE ALLERGIC PATIENT. Harold A. Abramson, M.D., with a panel discussion. 81 pages. The Bruce Publishing Company, St. Paul and Minneapolis, 1948. Price $2.50.

This little volume represents the panel discussion at a meeting of the American College of Allergists.

It is interesting reading and sheds light upon the role of allergy during the life of Hippocrates. Among the discussers Drs. Murray Peshkin, Sandor Rado and Edward Weiss contribute interesting facts.

Physicians who are interested in the allergic and psychosomatic aspects of disease, will find useful information between the covers of this little book.

YEAR BOOK OF DRUG THERAPY. Harry Beckman, M.D., Director, Department of Pharmacology, Marquette University School of Medicine. 718 pages, illustrated. The Year Book Publishers, Chicago, Ill., 1949. Price $4.75.

This new volume supersedes the Year Book of Therapeutics and under the able editorship of Dr. Beckman fills a need in medical literature. The general practitioner as well as the specialist will find useful information gathered from the world's medical literature describing the use and application of drugs or other therapeutic measures in medicine including the various specialties, neuropsychiatry, obstetrics, ophthalmology, otolaryngology, pediatrics, roentgenology, surgical specialties and venereal diseases.

In looking over the table of contents one is impressed with the thoroughness of the material reviewed. Penicillin, aureomycin, streptomycin and dihydrostreptomycin and their application in treatment are enlightening.

With addition of the extensive authors and cross index, the book is well printed and illustrated. It is highly recommended.

GERIATRIC MEDICINE, THE CARE OF THE AGING AND THE AGED. Edward J. Stieglitz, M.S., M.D., F.A.C.P., Attending Internist, Suburban Hospital, Bethesda, Md. Second edition, 773 pages. W. B. Saunders Company, Philadelphia, Pa., 1949. Price $12.00.

Forty-seven contributors, including the editor, contributed to this volume on "Geriatric Medicine". With the increased span of life more and more men and women live to a ripe old age, and the physician has to be well versed in the treatment of the various conditions arising in the individuals. Like the pediatrician, the physician who specializes in geriatrics or whose general practice includes these oldsters, will find useful information in Dr. Stieglitz's book.

Medical, surgical, physical and nutritional problems and their practical application in a given case are discussed by the various contributors. Gastrointestinal, cardiovascular, respiratory and nutritional problems, vitamin deficiencies, as well as the indications and contraindications for surgery, receive special attention.

Diet and drug therapy add to the value of this volume.

Dr. Stieglitz and the publishers are to be congratulated on bringing out a book so well written and printed.

PRACTICAL PHYSIOLOGICAL CHEMISTRY. Philip B. Hawk, Ph.D., President, and Bernard L. Oser, Ph.D., Director, Food Research Laboratories, New York; and William H. Summerson, Ph.D., Associate Professor of Biochemistry, Cornell University Medical College. 1323 pages, illustrated, Twelfth Edition. The Blakiston Company, Philadelphia, Pa., 1947. Price $10.00.

When a book reaches twelve editions there is not a question in the mind of the reviewer that "Practical Physiological Chemistry" has been a standard in its field since 1907. In this edition there is a complete revision of the text and many chapters have been entirely rewritten. New tests, new experiments, the sulfa drugs and antibiotics as well as the various vitamins and their importance in nutrition have received due consideration.

The authors discuss in detail protein chemistry and visual and photometric methods of measurement. New procedures for blood and urine analysis are additional features.

In addition to the thirty chapters, an appendix dealing with useful information completes the volume. It should be in the library of every physician.

THE YEAR BOOK OF GENERAL SURGERY. Evarts H. Graham, M.D., Professor of Surgery, Washington University School of Medicine, St. Louis, Mo. 707 pages. The Year Book Publishers, Chicago, Ill., 1949. Price $4.75.

One need not be a surgeon to read the 1949 Year Book of General Surgery, because within its pages the reader will find discussion of the more recent advances in surgical procedure.

The Editor, Dr. Graham, needs no introduction to the medical profession. Under his able guidance, this year's review of the literature covers the entire field of surgery including the role of antibiotics and chemotherapy.

A more than interesting chapter, dealing with the newer armamentarium and its application in surgery, adds to the value of the well printed and illustrated volume.

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1. Gastroenterology 3:54, 1944
2. Am. J. Roentgenol. 19:341, 1928
3. J. Lab. and Clin. Med. 18:1016, 1933
4. J. Lab. and Clin. Med. 19:567, 1934

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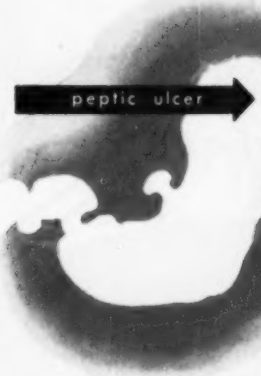

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Hubscher, O., Lancet, **251, 272 (1946).*

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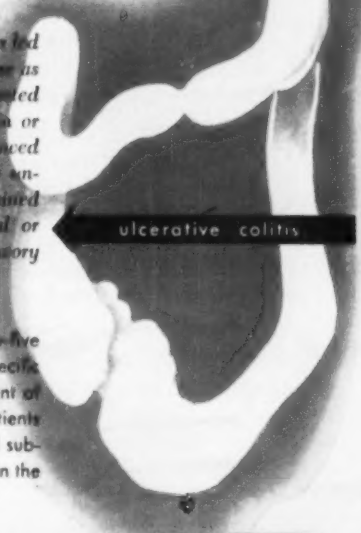
*Rivers, A. D., Am. J. Dig. Dis., **2**, 189 (1935).



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Gill, A. M., Lancet, **2, (1945).*

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*Streicher, M. H., J. Lab. Clin. Med., **33**, 1633 (1948).

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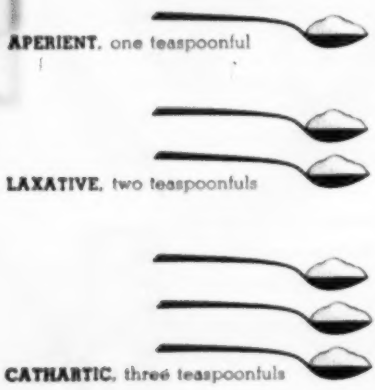

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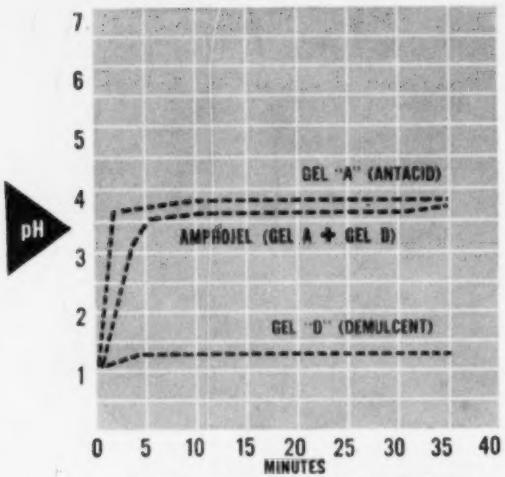

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